Access DB# 95698/ 96062

# SEARCH REQUEST FORM

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JUN - 3 2003

Requester's Full Name Jeffrey E. Russel Examiner # 62785 Date 6-3-2003

Art Unit 1654 Phone Number 308-3975 Serial Number (S09/815,978

Mail Box and Bldg Room Location CM1-11D13/CM1-9807 Results Format Preferred (circle) PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

**********

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention Hydrazine-Based And Carbonyl-Based Bifunctional Crosslinking Reagents

Inventors (please provide full names) D. Schwartz

Earliest Priority Filing Date 3-22-2001

*For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the following partial structures:

(A) $C_{1-20} - NH - \overset{(O\text{ or }S)}{\overset{\|}{C}} - NH - NH_2$

(B) $C_{1-20} - NH - NH - \overset{(O\text{ or }S)}{\overset{\|}{C}} - NH - NH_2$

keywords are crosslink?, bifunctional, heterobifunctional, immobili?, conjugat?.

Thank you.

JER

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STAFF USE ONLY

Searcher _____

Searcher Phone # _____

Searcher Location _____

Date Searcher Picked Up 6/4/03

Date Completed 6/6/03

Searcher Prep & Review Time 20 | 10

Clerical Prep Time _____

Online Time 30 | 10

Type of Search

NA Sequence (#) _____

AA Sequence (#) _____

Structure (#) 2

Bibliographic _____

Litigation _____

Fulltext _____

Patent Family _____

Other _____

Vendors and cost where applicable

STN 52

Dialog _____

Questel/Orbit _____

Dr. Link _____

Lexis/Nexis _____

Sequence Systems _____

WWW/Internet _____

Other (specify) _____

=> d ibib abs hitstr 14 1-5

L4 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 200[illegible] HCAPLUS
DOCUMENT NUMBER: 137:[illegible]
TITLE: Ternary biomolecule/polymer/surface-based immobilization methods
INVENTOR(S): **Schwartz, David A.**
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002057412 | A2 | 20020725 | WO 2002-US1161 | 20020116 |
| WO 2002057412 | A3 | 20030206 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 20021465[illegible] | A1 | 20021010 | US 2001-50277 | 20020115 |
| PRIORITY APPLN. INFO.: | | | US 2001-260094P | P 20010116 |
| | | | US 2002-50277 | A 20020115 |
| | | | US 2000-191186P | P 20000322 |

AB Immobilizing natural or synthetic biomols. onto surfaces comprises covalently linking the natural or synthetic biomol. to a mono- or bi-functional polymer and covalently and/or electrostatically immobilizing the biomol./polymer conjugate to an unmodified or modified surface, where the biomol. is an oligonucleotide, a polynucleotide, a protein, a glycoprotein, a peptide or a carbohydrate that was modified to incorporate .gtoreq.1 nucleophilic groups comprising an aliph. or arom. amino, thiol, **hydrazine**, thiosemicarbazide, hydrazide, thiocarbazide, carbazide, aminoxy, a deriv. of 2-hydrazinopyridine or aminoxyacetic acid or .gtoreq.1 electrophilic groups comprising an aliph. or arom. aldehyde, ketone, epoxide, isocyanate, isothiocyanate, succinimidyl ester or cyanuric chloride or a linkable arom. aldehyde or ketone and the surface was modified to possess either neutral, cationic or anionic groups or a combination neutral, anionic and/or cationic moieties.

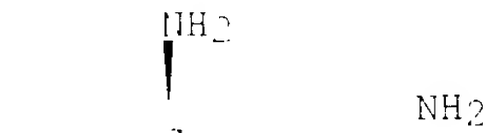
IT **25104-18-1DP**, Polylysine, reaction products with succinimidyl hydrazinonicotinate acetone hydrazone, conjugates **38000-06-5DP**, Polylysine, reaction products with succinimidyl hydrazinonicotinate acetone hydrazone, conjugates **60444-78-2DP**, Succinimidyl 4-formylbenzoate, reaction products with polylysine, conjugates with oligonucleotides **362522-50-7DP**, Succinimidyl 6-hydrazinonicotinate acetone hydrazone, polymer deriv., conjugates with oligonucleotides
RL: BUU (Biological use, unclassified); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ternary biomol./polymer/surface-based immobilization systems)

RN 25104-18-1 HCAPLUS
CN L-Lysine, homopolymer (9CI) (CA INDEX NAME)

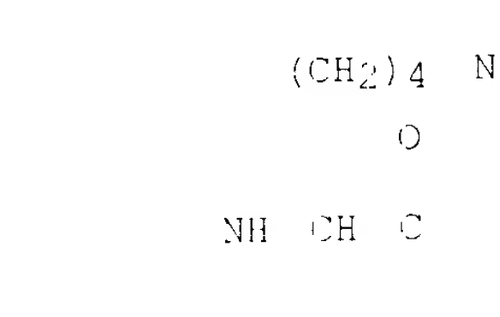
CM 1

CRN 56-87-1
CMF C6 H14 N2 O2

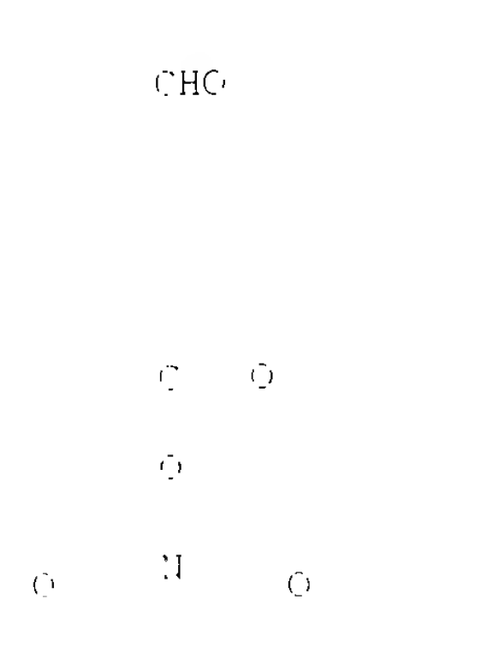
Absolute stereochemistry.



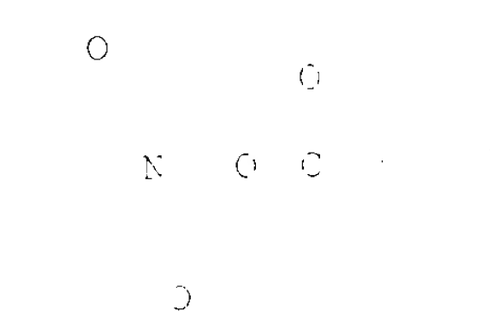
RN 38000-06-5 HCAPLUS
CN Poly[imino[(1S)-1-(4-aminobutyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



RN 60444-78-2 HCAPLUS
CN Benzaldehyde, 4-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]- (9CI) (CA INDEX NAME)



RN 62522-50-7 HCAPLUS
CN 1,5-Pyrrolidinedione, 1-[[[1,6-dihydro-6-[(1-methylethylidene)hydrazono]-3-pyridinyl]carbonyl]oxy]- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS
ACCESSION NUMBER: 2001:713305 HCAPLUS
DOCUMENT NUMBER: 135:272864
TITLE: **Hydrazine**-based and carbonyl-based bifunctional crosslinking reagents for biomolecules, drugs, and synthetic polymers
INVENTOR(S): **Schwartz, David A.**
PATENT ASSIGNEE(S): Cellulink, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001070685 | A2 | 20010927 | WO 2001-US9252 | 20010322 |
| WO 2001070685 | A3 | 20030327 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 20030013857 | A1 | 20030116 | US 2001-815973 | 20010322 |
| EP 1315699 | A2 | 20030604 | EP 2001-920666 | 20010322 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

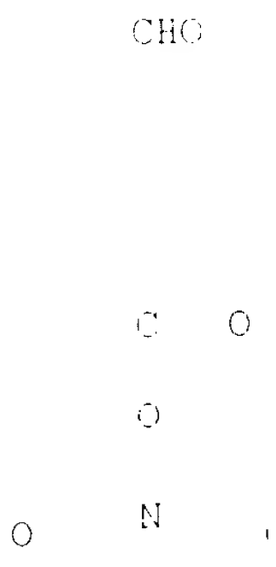
| | | |
|---|---|---|
| PRIORITY APPLN. INFO.: | US 2000-191868P | P 20000322 |
| | WO 2001-US9252 | W 20010322 |

OTHER SOURCE(S): MARPAT 135:272864
AB Reagents and methods are provided for bifunctional crosslinking and immobilizing biomols., drugs, and synthetic polymers. The reagents of formula BFAUHNH2.bul.HX [wherein A = NHCO, NHCS, NHNHCO, NHNHCS, or a direct bond; B = an amino or thio reactive moiety; F = specified aligh. divalent groups contg. any combination of cycloalkylene, C(R10)2, CR10:CR10, C:CR12R13, CR12R13, C.tplbond.C, O, SGa, NR10, N+R12R13, CL, etc.; a = 0-1; b = 0-3; G = O or NR10; L = S, O, or NR10; R10 = specified monovalent groups; R12 and R13 = independently H, (cyclo)alkyl, alkenyl, alkynyl, or (hetero)aryl; or R12 and R13 together from (cyclo)alkylene or alkenylene; X = neg. counterion; or a deriv. thereof] possess a thiol or amine reactive group and a hydrazine or oxyamine moiety. Conjugates and immobilized biomols. are also provided. For example, hydrazinonicotinic acid was converted to the acetone hydrazone and treated with N-hydroxysuccinimide to give the crosslinking agent, succinimidyl 6-hydrazinonicotinate acetone hydrazone (I), in 33% yield. A soln. of ovalbumin in PBS and EDTA was added to a soln. of I in DMF and the mixt. incubated at room temp. for 4 h to afford the **hydrazine**-modified protein, which exhibited a molar extinction coeff. of 22,000 at 360 nm.

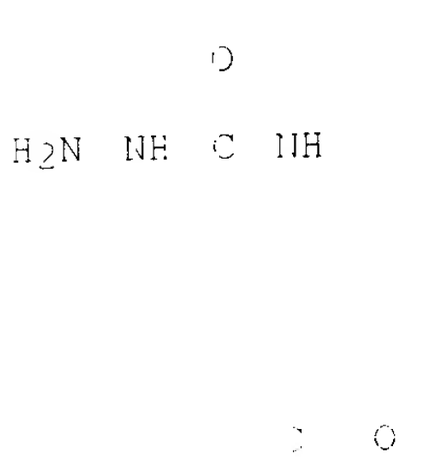
IT **60444-78-2 362522-64-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(crosslinking agent; prepn. of **hydrazine**- and carbonyl-based bifunctional crosslinking agents and use with biomols., drugs, and synthetic polymers)

RN 60444-78-2 HCAPLUS

CN Benzaldehyde, 4-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]- (9CI) (CA INDEX NAME)



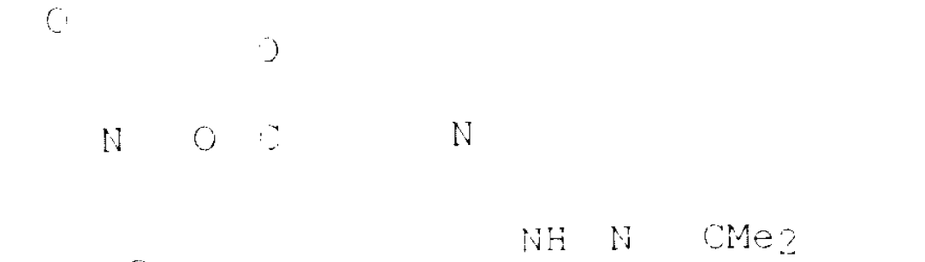
RN 362522-64-3 HCAPLUS
CN Hydrazinecarboxamide, N-[4-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

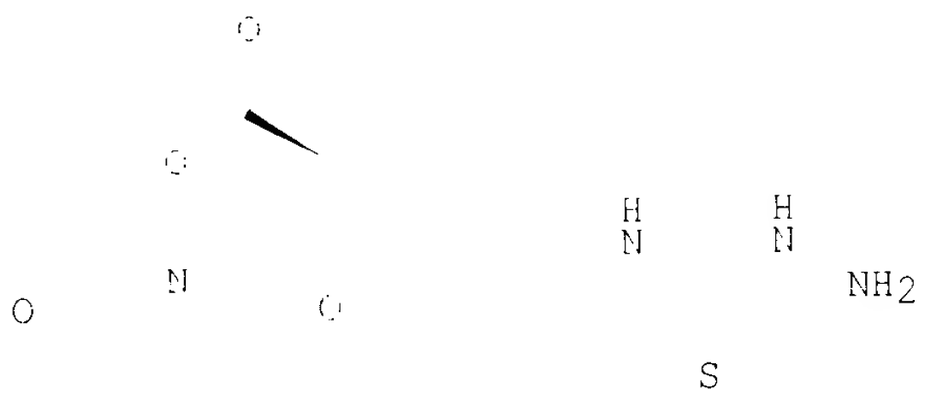
IT **362522-50-7P 362522-51-8P 362522-52-9P**
**362522-53-0P 362522-54-1P 362522-55-2P**
**362522-56-3P 362522-57-4P 362522-58-5P**
RL: FCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crosslinking agent; prepn. of **hydrazine**- and carbonyl-based bifunctional crosslinking agents and use with biomols., drugs, and synthetic polymers)

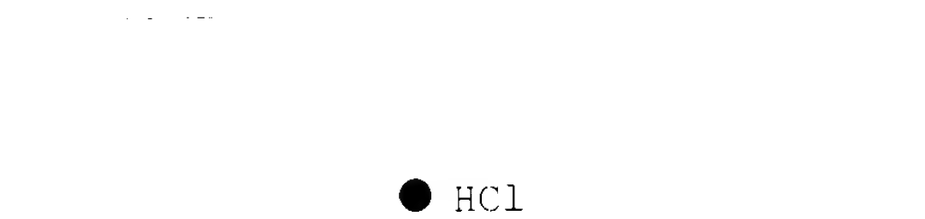
RN 362522-50-7 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[[1,6-dihydro-6-[(1-methylethylidene)hydrazono]-3-pyridinyl]carbonyl]oxy]- (9CI) (CA INDEX NAME)



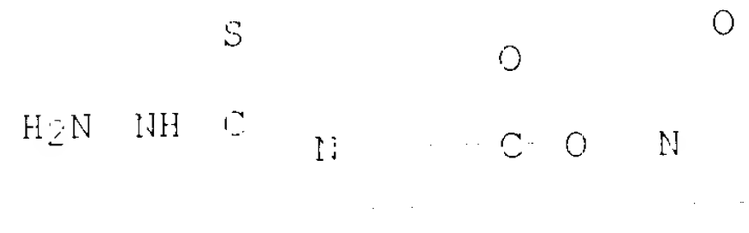
RN 362521-51-8 HCAPLUS
CN Hydrazinecarbothioamide, N-[[trans-4-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]cyclohexyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

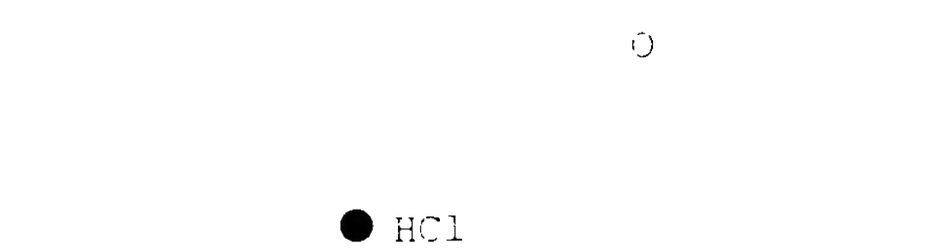
Relative stereochemistry.



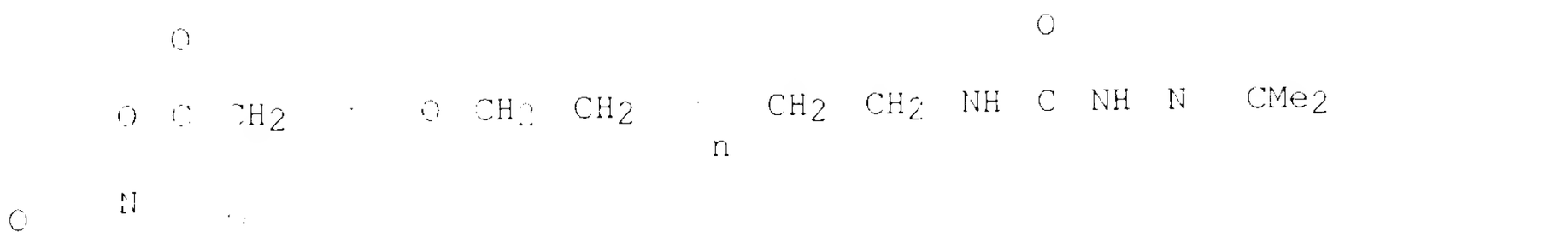


RN 362522-52-9 HCAPLUS
CN 1-Pyrrolidinecarbothioic acid, 3-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-, hydrazide, monohydrochloride (9CI) (CA INDEX NAME)

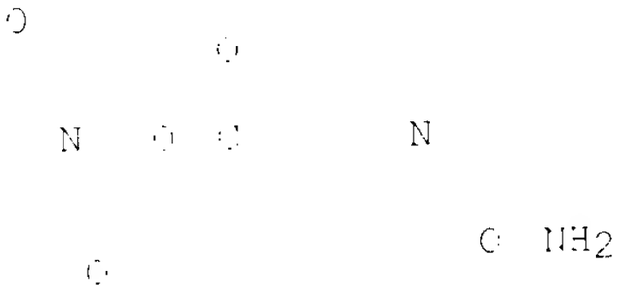


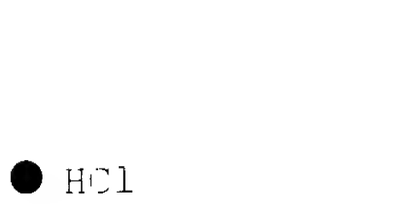


RN 362522-53-0 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethyl]-.omega.-[2-[[[(1-methylethylidene)hydrazino]carbonyl]amino]ethyl]- (9CI) (CA INDEX NAME)

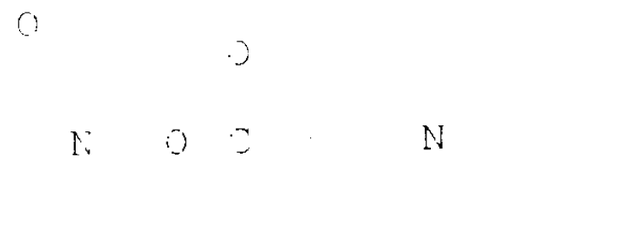


RN 362252-54-1 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[[6-(aminooxy)-3-pyridinyl]carbonyl]oxy]-, monohydrochloride (9CI) (CA INDEX NAME)

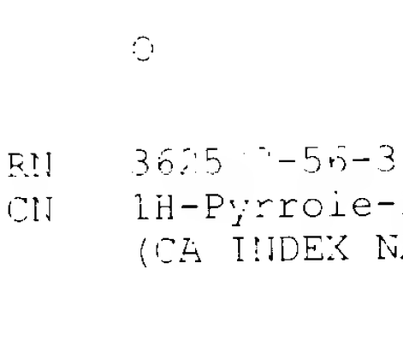




RN 362252-55-2 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[[6-[[(1-methylethylidene)amino]oxy]-3-pyridinyl]carbonyl]oxy]- (9CI) (CA INDEX NAME)

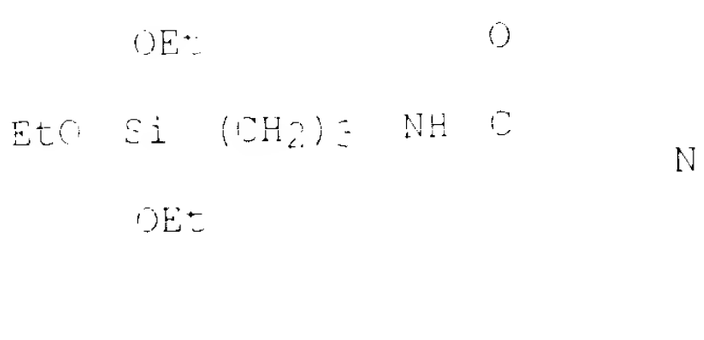


RN 362252-56-3 HCAPLUS
CN 1H-Pyrrole-2,5-dione, 1-[4-[[(1-methylethylidene)amino]oxy]phenyl]- (9CI) (CA INDEX NAME)



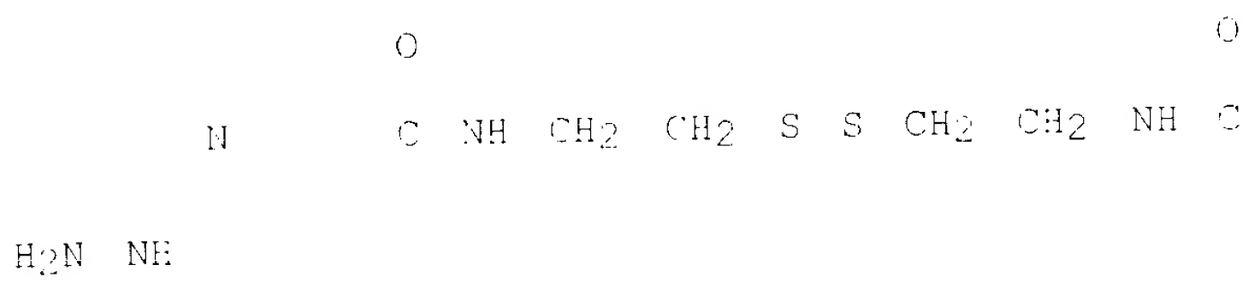
RN 362252-57-4 HCAPLUS

CN 3-Pyridinecarboxamide, 6-[(1-methylethylidene)hydrazino]-N-[3-(triethoxysilyl)propyl]- (9CI) (CA INDEX NAME)



RN 362522-58-5 HCAPLUS
CN 3-Pyridinecarboxamide, N,N'-(dithiodi-2,1-ethanediyl)bis[6-hydrazino-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



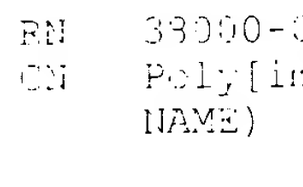
●2 HCl

PAGE 1-B

IT **302-01-2DP, Hydrazine**, derivs., preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crosslinking agents; prepn. of **hydrazine**- and carbonyl-based bifunctional crosslinking agents and use with biomols., drugs, and synthetic polymers)
RN 302-01-2 HCAPLUS
CN Hydrazine (7CI, 8CI, 9CI) (CA INDEX NAME)

IT **6066-82-6**, N-Hydroxysuccinimide **25104-18-1**, Poly-L-lysine **38000-06-5**, Poly-L-lysine **133081-24-0**, 6-Hydrazinonicotinic acid **363633-70-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of **hydrazine**- and carbonyl-based bifunctional crosslinking agents and use with biomols., drugs, and synthetic

polymers)
RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)

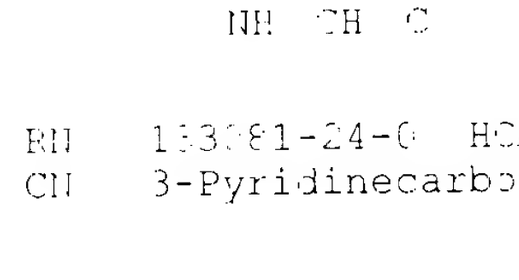


RN 25104-18-1 HCAPLUS
CN L-Lysine, homopolymer (9CI) (CA INDEX NAME)

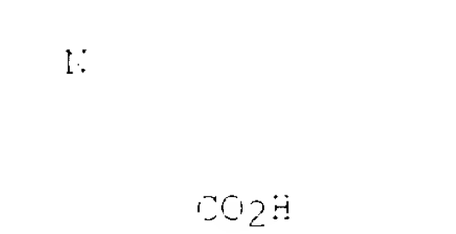
CM 1

CRN 56-87-1
CMF C6 H14 N2 O2

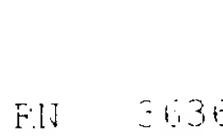
Absolute stereochemistry.

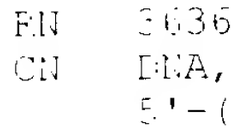


RN 38000-06-5 HCAPLUS
CN Poly[imino[(1S)-1-(4-aminobutyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



RN 133181-24-0 HCAPLUS
CN 3-Pyridinecarboxylic acid, 6-hydrazino- (9CI) (CA INDEX NAME)





RN 363633-70-9 HCAPLUS
CN DNA, d(T-T-T-T-T-T-T-A-G-C-C-T-A-A-C-T-G-A-T-G-C-C-A-T-G), 5'-(6-aminohexyl hydrogen phosphate) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **25104-18-1DP**, Poly-L-lysine, hydrazinonicotinamide modified
**38000-06-5DP**, Poly-L-lysine, hydrazinonicotinamide modified
**364163-70-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)

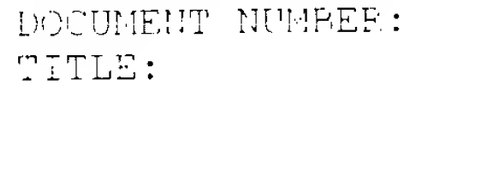
(prepn. of **hydrazine**- and carbonyl-based bifunctional crosslinking agents and use with biomols., drugs, and synthetic polymers)

RN 25104-18-1 HCAPLUS
CN L-Lysine, homopolymer (9CI) (CA INDEX NAME)

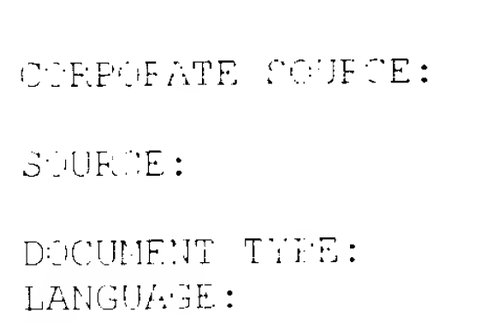
CM 1

CRN 56-87-1
CMF C6 H14 N2 O2

Absolute stereochemistry.



RN 30000-06-9 HCAPLUS
CN Poly[imino[(1S)-1-(4-aminobutyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)



RN 30416G-70-2 HCAPLUS
CN DNA, d(T-T-T-T-T-T-T-A-G-C-C-T-A-A-C-T-G-A-T-G-C-C-A-T-G), 5'-[6-[(4-formylbenzoyl)amino]hexyl hydrogen phosphate] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

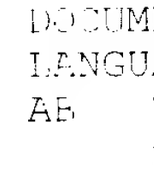
L4 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:602039 HCAPLUS
DOCUMENT NUMBER: 115:202039
TITLE: Preparation of hydrazine-modified proteins and their use for the synthesis of technetium-99m-protein conjugates
AUTHOR(S): **Schwartz, David A.**; Abrams, Michael J.; Hauser, Marguerite M.; Gaul, Forrest E.; Larsen, Scott K.; Rauh, Donald; Zubieta, Jon A.
CORPORATE SOURCE: Johnson Matthey Pharm. Res., West Chester, PA, 19380-1497, USA
SOURCE: Bioconjugate Chemistry (1991), 2(5), 333-6
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The syntheses and protein linking properties of succinimidyl 4-hydrazinobenzoate hydrochloride (SHBH) and succinimidyl 6-hydrazinonicotinate hydrochloride (SHNH), two new heterobifunctional linkers which lead to hydrazino-modified proteins, are described. SHBH-modified proteins are unstable due to the presence of the **phenylhydrazine** moiety. This problem was overcome by synthesizing the hydrazinopyridine analog SHNH, and the conjugates derived from this

linker are stable. Tc(V) oxo precursors readily add to hydrazinopyridine-modified proteins to yield the desired 99mTc-radiolabeled protein. 99mTc-hydrazinopyridine-polyclonal IgG conjugates are useful agents for the imaging of focal sites of infection.

IT **6066-82-6**, N-Hydroxysuccinimide
PL: RCT (Reactant); FACT (Reactant or reagent)
(esterification of, with hydrazinobenzoic acid deriv.)

RN 6066-82-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1991:181413 HCAPLUS

DOCUMENT NUMBER: 114:181413

TITLE: Technetium-99m-human polyclonal IgG radiolabeled via the hydrazino nicotinamide derivative for imaging focal sites of infection in rats

AUTHOR(S): Abrams, Michael J.; Juweid, Malik; TenKate, Caroline I.; **Schwartz, David A.**; Hauser, Marguerite M.; Gaul, Forrest E.; Fuccello, Anthony J.; Rubin, Robert H.; Strauss, H. William; Fischman, Alan J.

CORPORATE SOURCE: Dep. Radiol., Massachusetts Gen. Hosp., Boston, MA, USA

SOURCE: Journal of Nuclear Medicine (1990), 31(12), 2022-8
CODEN: JNMEAQ; ISSN: 0161-5505

DOCUMENT TYPE: Journal

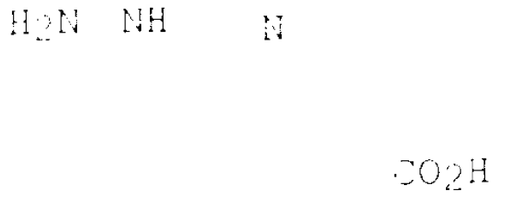
LANGUAGE: English

AB The biol. behavior of human polyclonal IgG radiolabeled with 99mTc, by a novel method, via a nicotinyl **hydrazine** deriv., was evaluated in rats. Technetium-99m- and indium-111-IgG were coadministered to normal rats and biodistribution was detd. at 2, 6, and 16 h. The inflammation imaging properties of the 2 reagents were compared in rats with deep-thigh infection due to Escherichia coli. Blood clearance of both antibody preps. was well described by a biexponential function: (99mTc-IgG: t1/2 = 3.82 and 57.52 h, 111In-IgG: 3.93 and 40.71 h). Biodistributions in the solid organs were similar; however, small but statistically significant differences were detected: 99mTc-IgG > 111In-IgG in lung, liver, and spleen; 99mTc-IgG < 111In-IgG in kidney and skeletal muscle. At all 3 imaging times, target-to-background ratio and percent residual activity for the 2 compds. were remarkably similar. These studies establish that human polyclonal IgG labeled with 99mTc via a nicotinyl **hydrazine** modified intermediate is equiv. to 111In-IgG for imaging focal sites of infection in exptl. animals.

IT **133081-24-0P**
PL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and butoxylation)

RN 133081-24-0 HCAPLUS

CN 3-Pyridinecarboxylic acid, 6-hydrazino- (9CI) (CA INDEX NAME)

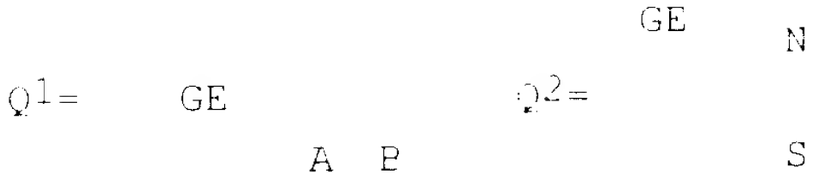


L4 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:164011 HCAPLUS
DOCUMENT NUMBER: 114:164011
TITLE: Preparation of succinimido hydrazinoarylcarboxylates and analogs as conjugating agents for biological macromolecules
INVENTOR(S): **Schwartz, David A.**; Abrams, Michael J.; Giandomenico, Christen M.; Zubieta, Jan A.
PATENT ASSIGNEE(S): Johnson Matthey PLC, UK
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 384769 | A2 | 19900829 | EP 1990-301949 | 19900223 |
| EP 384769 | A3 | 19911127 | | |
| EP 384769 | B1 | 19960424 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL | | | | |
| ZA 9001283 | A | 19910327 | ZA 1990-1283 | 19900220 |
| NO 9000838 | A | 19900827 | NO 1990-838 | 19900221 |
| NO 178186 | B | 19951030 | | |
| NO 178186 | C | 19960207 | | |
| AU 9050074 | A1 | 19900913 | AU 1990-50074 | 19900223 |
| AU 630668 | B2 | 19921105 | | |
| CA 2010800 | AA | 19900824 | CA 1990-2010800 | 19900223 |
| CA 2010800 | C | 20010116 | | |
| HU 53600 | A2 | 19901128 | HU 1990-970 | 19900223 |
| HU 207995 | B | 19930329 | | |
| JP 03027356 | A2 | 19910205 | JP 1990-41389 | 19900223 |
| JP 2973997 | B2 | 20000807 | | |
| FI 95907 | B | 19951229 | FI 1990-948 | 19900223 |
| FI 95907 | C | 19960410 | | |
| AT 137219 | E | 19960515 | AT 1990-301949 | 19900223 |
| ES 2088690 | T3 | 19960816 | ES 1990-301949 | 19900223 |
| US 5306370 | A | 19940427 | US 1992-866282 | 19920408 |
| US 5420285 | A | 19950530 | US 1993-26426 | 19930304 |
| US 5750670 | A | 19980519 | US 1995-384641 | 19950206 |
| US 6117845 | B1 | 20000912 | US 1997-969148 | 19971112 |

PRIORITY APPLN. INFO.: US 1989-315279 A 19890223
US 1990-483,401 B1 19900221
US 1992-866,282 A3 19920408
US 1993-26426 A3 19930304
US 1995-384641 A3 19950206

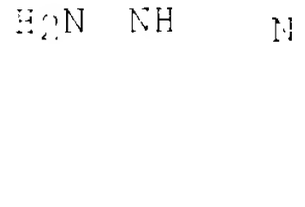
OTHER SOURCE(S): MARPAT 114:164011
GI



AB P3DNRNH.HX, R3DNRN:CR1R2, and R4NRN:CR1R2 (D = bond, CH2, CO, CSNH; R, R1, R2 = H, alkyl; R3 = aryl group Q1; A, B = CH, N; E = CO; G = group readily replaced by a primary amine; EG = maleimido; R4 = thiazolyl group Q2; X = anion) were prepd. Thus, 4-(HO2C)C6H4NHNH2 was N-protected and the product condensed with N-hydroxysuccinimide to give, after deprotection 4-(R5O2C)C6H4NHNH2.HCl (R5 = succinimido) which was conjugated with IgG and the product labeled with 99mTc. The latter gave infected/normal muscle distribution ratio of 6.3 when injected into rats having a hind leg abscess.

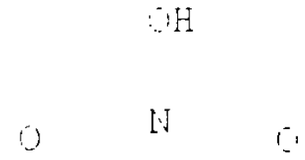
IT **133081-24-0P**
PL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of conjugating agents for biol. macromols.)

RN 133081-24-0 HCAPLUS
CN 2-Pyridinecarboxylic acid, 6-hydrazino- (9CI) (CA INDEX NAME)



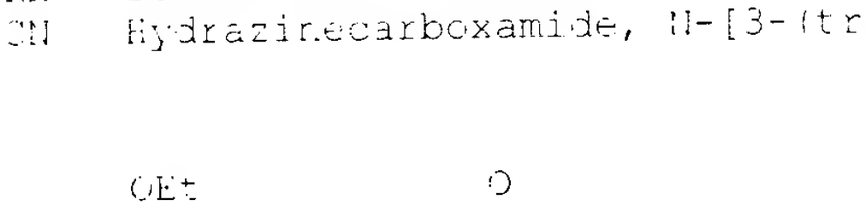
IT **6066-82-6**, N-Hydroxysuccinimide
PL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of conjugating agents for biol. macromols.)

RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



=> d ikib abs hitstr 19 1-38

L9 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:67164 HCAPLUS
DOCUMENT NUMBER: 134:265
TITLE: Attachment of benzaldehyde-modified oligodeoxynucleotide probes to semicarbazide-coated glass
AUTHOR(S): Podyminogin, Mikhail A.; Lukhtanov, Eugeny A.; Reed, Michael W.
CORPORATE SOURCE: Epoch Biosciences, Bothell, WA, 98021, USA
SOURCE: Nucleic Acids Research (2001), 29(24), 5090-5098
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Attachment of oligodeoxynucleotides (ODNs) contg. benzaldehyde (BAL) groups to semicarbazide-coated glass (SC-glass) slides is described. 5'-BAL-ODNs are prepd. using automated DNA synthesis and an acetal-protected BAL phosphoramidite reagent. The hydrophobic protecting group simplifies purifn. of BAL-ODNs by reverse phase HPLC and is easily removed using std. acid treatment. The electrophilic BAL-ODNs are stable in soln., but react specifically with semicarbazide groups to give semicarbazide silane to give SC-glass. BAL-ODNs are coupled to the SC-glass surface by a simple one-step procedure that allows rapid, efficient and stable attachment. Hand-spotted arrays of BAL-ODNs were prepd. to evaluate loading d. and hybridization properties of **immobilized** probes. Hybridization to radiolabeled target strands shows that at least 30% of the coupled ODNs were available for hybridization at max. **immobilization** d. The array was used to probe single nucleotide polymorphisms in synthetic DNA targets, and PCR products were correctly genotyped using the same macroarray. Application of this chem. to manuf. of DNA microarrays for sequence anal. is discussed.
IT **106868-88-6P**
RL: RCT (Reactant); SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(attachment of benzaldehyde-modified oligodeoxynucleotide probes to semicarbazide-coated glass)
RN 106868-88-6 HCAPLUS
CN Hydrazinecarboxamide, N-[3-(triethoxysilyl)propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:843748 HCAPLUS
DOCUMENT NUMBER: 135:371103
TITLE: Water dispersion compositions useful as coatings of metals especially automobiles
INVENTOR(S): Yamauchi, Toyoaki; Takanohashi, Hiroaki; Takada, Yoshihiko

PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

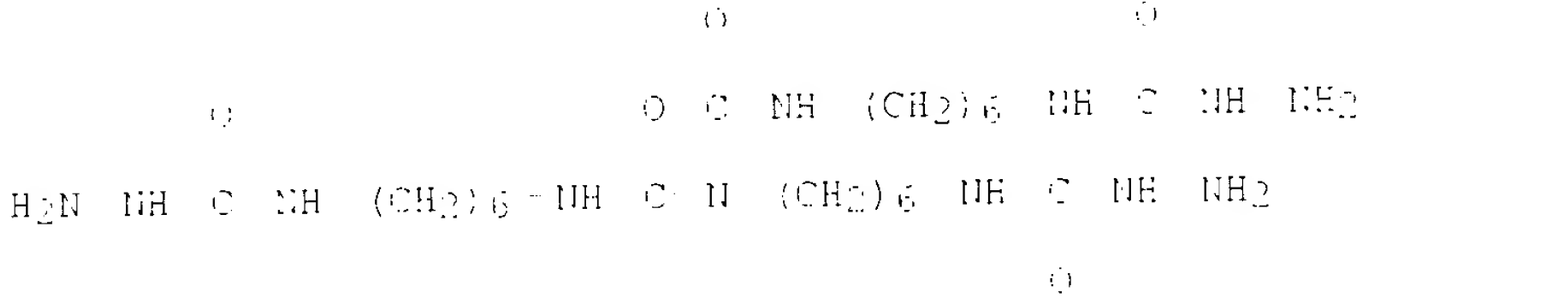
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2001323123 | A | 20011120 | JP 2000-139946 | 20000512 |
| | | | JP 2000-139946 | 20000512 |

PRIORITY APPLN. INFO.:

AB Title compns. comprise (i) carbonyl group-contg. aq. film forming resins comprising aq. polycarbonyl compds. and (ii) thermal **crosslinking** agents. The compns. are useful as intermediate and/or top base coatings for automobiles, esp. as three coat-one bake, and give coating films with good appearance. Thus, (a) an intermediate water resistant coating compn., (b) a white top base water resistant coating compn. comprising aq. polycarbonyl compd. obtained from Bu acrylate, diacetone acrylamide, 2-hydroxyethyl methacrylate, methacrylic acid, Me methacrylate, styrene, 2,2-azobis(2,4-dimethylvaleronitrile), and N,N-dimethylethanolamine, aq. film forming resin obtained from Bu acrylate, diacetone acrylamide, 2-hydroxyethyl methacrylate, Latemul S 180A, methacrylic acid, Me methacrylate, trimethylolpropane triacrylate, N,N-dimethylethanolamine, and ammonia, and Cymel 254, and (c) an acrylic clear coating compn. were applied on an electrodeposited coated plate (wet on wet method), electrostatically coated, and baked at 150.degree. for 25 min to give a coating film with good appearance.

IT **175870-12-9P**
PL: IMF (Industrial manufacture); MOA (Modifier or additive use); PREP (Preparation); USES (Uses)
(water dispersion intermediate and/or top base coating compns. giving cured coating films with good appearance)

RN 175870-12-9 HCAPLUS
CN 1,9,11,13,20-Pentaazaheneicosanedioic acid, 11-[6-[(hydrazinocarbonyl)amino]hexyl]-10,12-dioxo-, dihydrazide (9CI) (CA INDEX NAME)



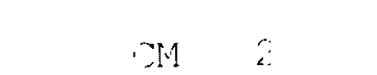
IT **374620-65-2P 374620-67-4P 374620-76-5P**
PL: IMF (Industrial manufacture); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(water dispersion intermediate and/or top base coating compns. giving cured coating films with good appearance)

RN 374620-65-2 HCAPLUS
CN 1,9,11,13,20-Pentaazaheneicosanedioic acid, 11-[6-[(hydrazinocarbonyl)amino]hexyl]-10,12-dioxo-, dihydrazide, polymer with butyl 2-propenoate, N-(1,1-dimethyl-3-oxobutyl)-2-propenamide, ethenylbenzene, 2-ethyl-2-[[(1-oxo-2-propenyl)oxy]methyl]-1,3-propanediyl di-2-propenoate, formaldehyde, 2-hydroxyethyl 2-methyl-2-propenoate, Latemul S 180A, methyl 2-methyl-2-propenoate, 2-methyl-2-propenoic acid

and 1,3,5-triazine-2,4,6-triamine, ammonium salt, compd. with 2-(dimethylamino)ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 108-01-0
CMF C4 H11 N O

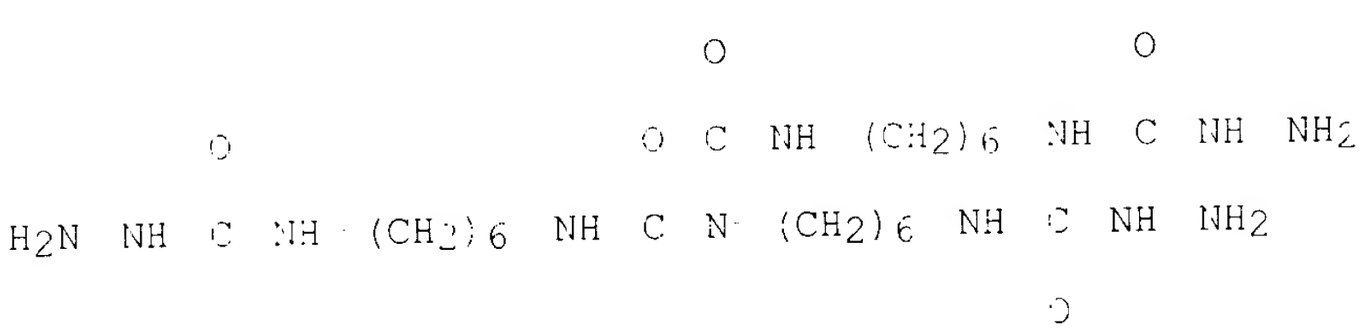


CM 2

CRN 374620-64-1
CMF (C23 H50 N12 O5 . C15 H20 O6 . C9 H15 N O2 . C8 H8 . C7 H12 O2 . C6 H10 O3 . C5 H8 O2 . C4 H6 O2 . C3 H6 N6 . C H2 O . Unspecified)x
CCI PMS

CM 3

CRN 175370-12-9
CMF C23 H50 N12 O5



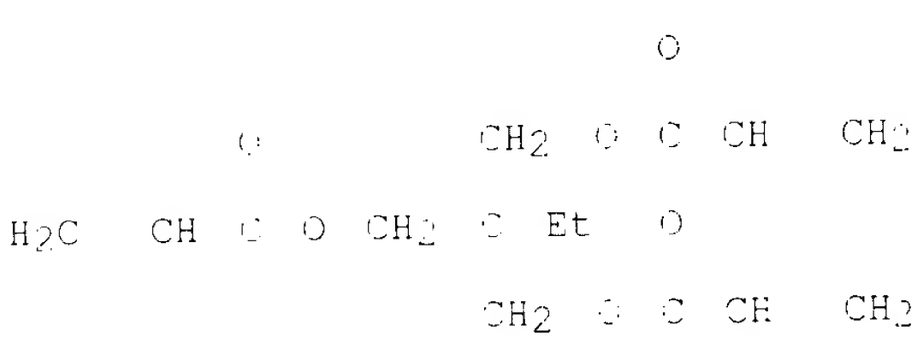
CM 4

CRN 113255-53-1
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

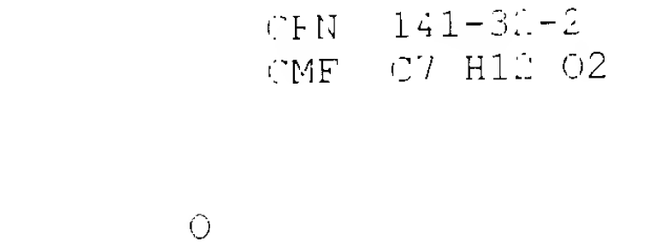
CM 5

CRN 15625-89-5
CMF C15 H20 O6



CM 6

CRN 2873-97-4
CMF C9 H15 N O2

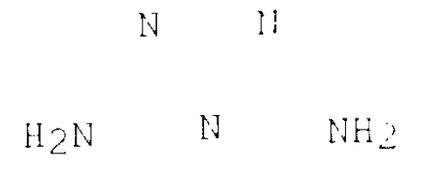


CM 7

CRN 868-77-9
CMF C6 H10 O3

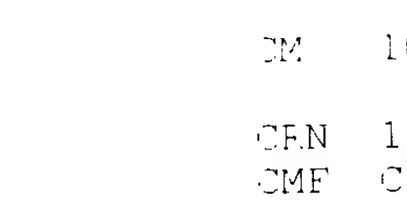
CM 8

CRN 141-32-2
CMF C7 H12 O2



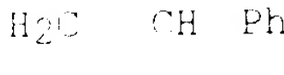
CM 9

CRN 108-78-1
CMF C3 H6 N6



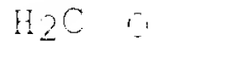
CM 10

CRN 100-42-5
CMF C8 H8



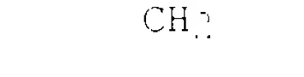
CM 11

CRN 80-62-6
CMF C5 H8 O2



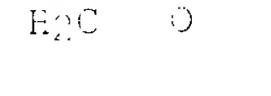
CM 12

CRN 79-41-4
CMF C4 H6 O2



CM 13

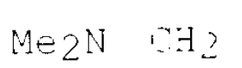
CRN 50-00-0
CMF C H2 O



ON 574620-67-4 HCAPLUS
CN 2,9,11,13,20-Pentaazaheneicosanedioic acid, 11-[6-[(hydrazinocarbonyl)amino]hexyl]-10,12-dioxo-, dihydrazide, polymer with butyl 2-propenoate, N-(1,1-dimethyl-3-oxobutyl)-2-propenamide, ethenylbenzene, formaldehyde, 2-hydroxyethyl 2-methyl-2-propenoate, Latemul S 180A, methyl 2-methyl-2-propenoate, 2-methyl-2-propenoic acid and 1,3,5-triazine-2,4,6-triamine, ammonium salt, compd. with 2-(dimethylamino)ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 108-01-0
CMF C4 H11 N O



CM 2

CRN 574620-66-3

CMF (C23 H50 N12 O5 . C9 H15 N O2 . C8 H8 . C7 H12 O2 . C6 H10 O3 . C5 H8 O4 . C4 H6 O2 . C3 H6 N6 . C H2 O . Unspecified)x

CCI EIN

CM 3

CRN 175370-12-9
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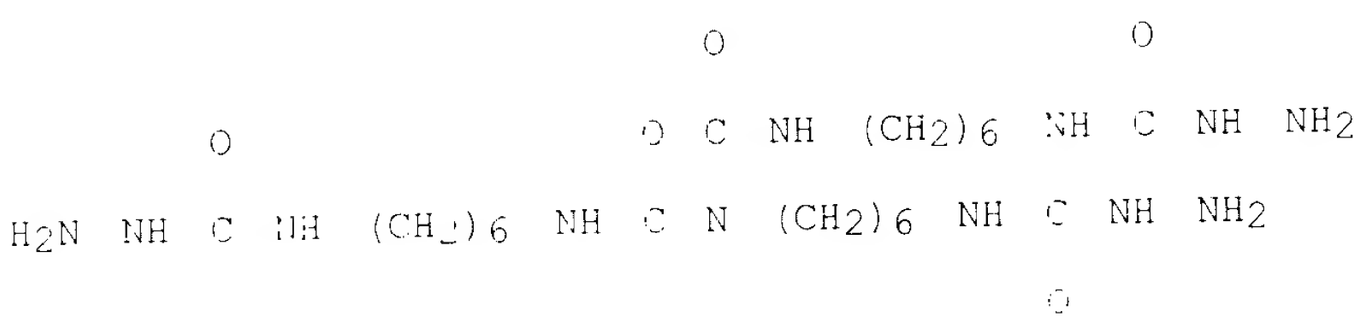

CM 4

CRN 111255-53-1
CMF Unspecified
CCI MAN

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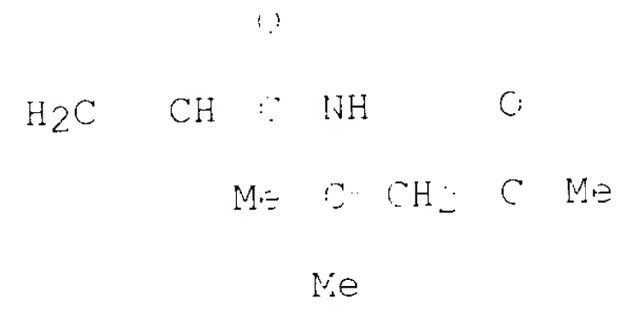
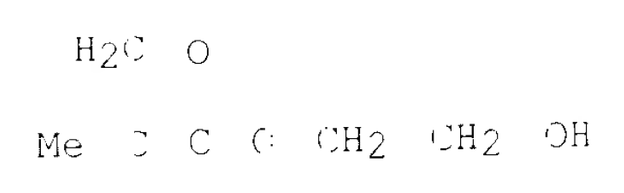
CM 5

CRN 2873-97-4
CMF C9 H15 N O2



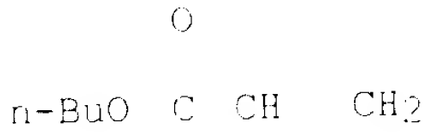
CM 6

CRN 868-77-9
CMF C6 H10 O3



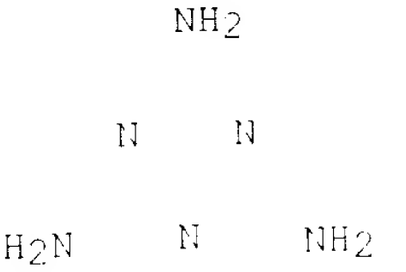
CM 7

CRN 141-32-2
CMF C7 H12 O2



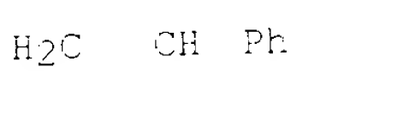
CM 8

CRN 108-78-1
CMF C3 H6 N6



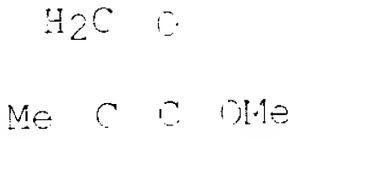
CM 9

CRN 100-42-5
CMF C8 H8



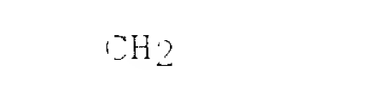
CM 10

CRN 80-62-6
CMF C5 H8 O2



CM 11

CRN 79-41-4
CMF C4 H6 O2



CM 12

CRN 50-00-0

CMF C H2 O

$H_2C$ O

RN 374620-76-5 HCAPLUS
CN 2,9,11,18,20-Pentaazaheneicosanedioic acid, 11-[6-[(hydrazinocarbonyl)amino]hexyl]-10,12-dioxo-, dihydrazide, polymer with butyl 2-propenoate, cyclohexyl 2-methyl-2-propenoate, N-(1,1-dimethyl-3-oxobutyl)-2-propenamide, formaldehyde, 2-hydroxyethyl 2-methyl-2-propenoate, Latemul S 180A, methyl 2-methyl-2-propenoate, 2-methyl-2-propenoic acid and 1,3,5-triazine-2,4,6-triamine, ammonium salt, compd. with 2-(dimethylamino)ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 108-01-0
CMF C4 H11 N O

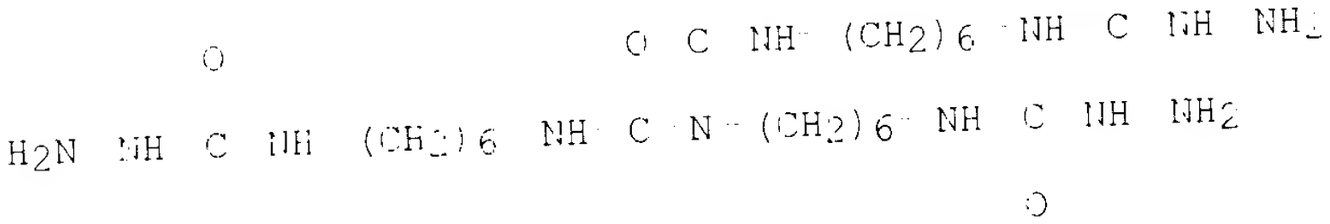
$Me_2N$ $CH_2$ $CH_2$ OH

CM 2

CRN 374620-75-4
CMF (C22 H50 N12 O5 . C10 H16 O2 . C9 H15 N O2 . C7 H12 O2 . C6 H10 O3 . C5 H8 O2 . C4 H6 O2 . C3 H6 N6 . C H2 O . Unspecified)x
CCI PMS

CM 3

CRN 108470-12-9
CMF C22 H50 N12 O5



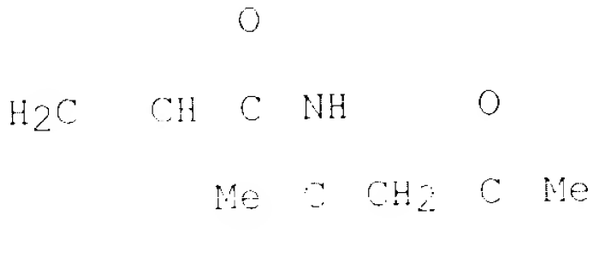
CM 4

CRN 113255-53-1
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 5

CRN 2873-97-4
CMF C9 H15 N O2

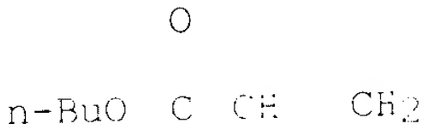


CM 6

CRN 363-77-9
CMF C6 H10 O3

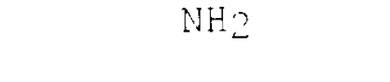
CM 7

CRN 141-32-2
CMF C7 H12 O2



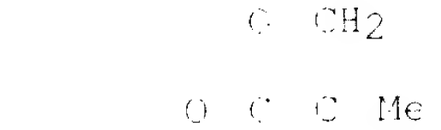
CM 8

CRN 108-78-1
CMF C3 H6 N6



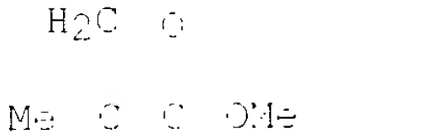
CM 9

CRN 101-43-9
CMF C10 H16 O2



CM 10

CRN 30-62-6
CMF C5 H8 O2

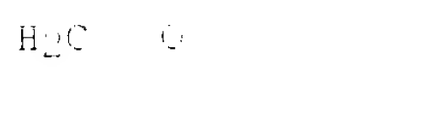


CM 11

CRN 79-41-4
CMF C4 H6 O2

CM 12

CRN 50-00-0
CMF C H2 O



L9 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:713305 HCAPLUS
DOCUMENT NUMBER: 135:272864
TITLE: Hydrazine-based and carbonyl-based **bifunctional crosslinking** reagents for biomolecules, drugs, and synthetic polymers
INVENTOR(S): Schwartz, David A.
PATENT ASSIGNEE(S): Solulink, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| WO 2001070685 | A2 | 20010927 | WO 2001-US9352 | 20010322 | |
| WO 2001070685 | A3 | 20020321 | | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| US 20030013857 | A1 | 20030116 | US 2001-915978 | 20010322 | |
| EP 1315699 | A2 | 20030604 | EP 2001-920666 | 20010322 | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

| | | | |
|---|---|---|---|
| | | US 2000-191136P | P 20000322 |
| | | WO 2001-US9252 | W 20010322 |

PRIORITY APPLN. INFO.:

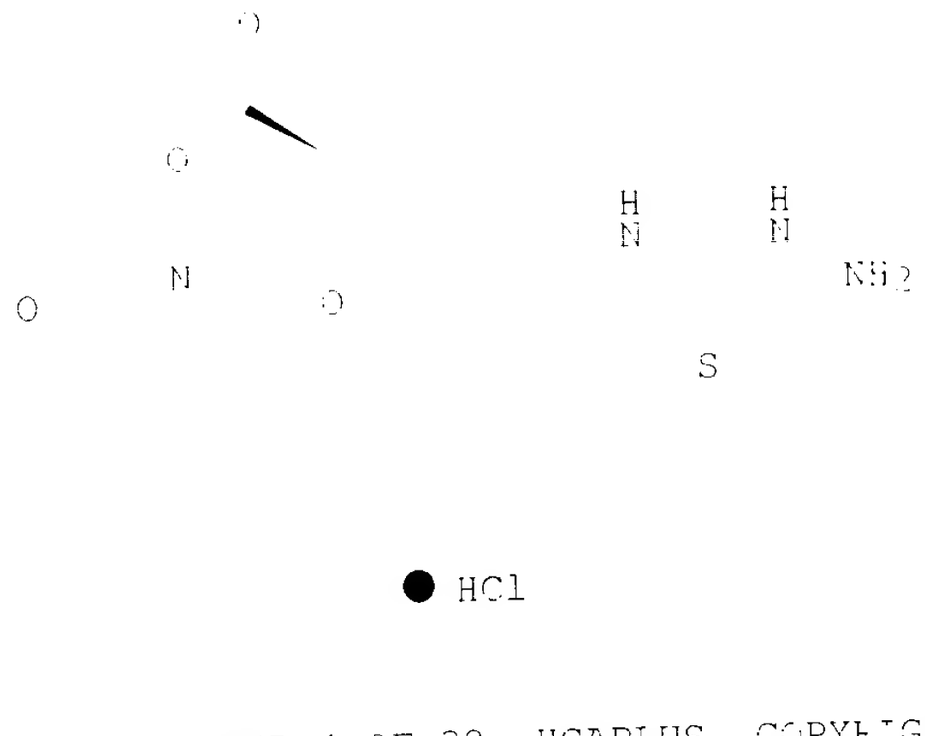
OTHER SOURCE(S): MARPAT 135:272864

AB Reagents and methods are provided for **bifunctional crosslinking** and **immobilizing** biomols., drugs, and synthetic polymers. The reagents of formula BPA:HNHR.bnl.HK [wherein A = NHCO, NHCS, NHNHCO, NHNHCS, or a direct bond; B = an amino or thio reactive moiety; F = specified aliph. divalent groups containing any combination of cycloalkylene, C(F10):CF10, CF10:CF10, C:CF12F13, CR12R13, C.tplbond.C, O, S(O)a, NF10, N-F12F13, CL, etc.; a = 0-2; r = 0-3; G = O or NF10; L = S, O, or NR10; R10 = specified monovalent groups; R12 and R13 = independently H, (cyclo)alkyl, alkenyl, alkynyl, or (hetero)aryl; or R12 and F13 together from (cyclo)alkylene or alkenylene; X = neg. counterion; or a deriv. thereof] possess a thiol or amino reactive group and a hydrazino or oxyamino moiety. **Conjugates** and **immobilized** biomols. are also provided. For example, hydrazinonicotinic acid was converted to the acetone hydrazone and treated with N-hydroxysuccinimide to give the **crosslinking** agent, succinimidyl 6-hydrazinonicotinate acetone hydrazone (I), in 43% yield. A soln. of I in DMF and soln. of ovalbumin in PBS and EDTA was added to a soln. of I in DMF and the mixt. incubated at room temp. for 4 h to afford the hydrazine-modified protein, which exhibited a molar extinction coeff. of 22,000 at 360 nm.

IT **362522-51-8P**
RL: BCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**crosslinking** agent; prepn. of hydrazine- and carbonyl-based **bifunctional crosslinking** agents and use with biomols., drugs, and synthetic polymers)

RN 362522-51-8 HCAPLUS
CN Hydrazinecarbothioamide, N-[[trans-4-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]cyclohexyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.




L9 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:147396 HCAPLUS
DOCUMENT NUMBER: 134:241166
TITLE: Preparation of a coating, a coated substrate, an adhesive, a film or sheet, and the coating mixture to be used
INVENTOR(S): Hesselmans, Laurentius Cornelius Josephus; Spek, Dirk Pieter
PATENT ASSIGNEE(S): Stahl International B.V., Neth.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001013451 | A2 | 20010405 | WO 2000-NL599 | 20000929 |
| WO 2001013451 | A3 | 20011025 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, ML, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| NL 1013179 | C2 | 20010402 | NL 1999-1013179 | 19990930 |
| EP 1133991 | A2 | 20010918 | EP 2000-970320 | 20000929 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| BR 2000014669 | A | 20021001 | BR 2000-14669 | 20000929 |
| JP 2003510431 | T2 | 20030318 | JP 2001-526598 | 20000929 |
| | | | NL 1999-1013179 A | 19990930 |
| | | | WO 2000-NL694 W | 20000929 |

PRIORITY APPLN. INFO.:

AB In this process, a mixt. of a polyisocyanate functional, a polyepoxide functional, a polyanhydride functional or a polyketone functional compd. or polymer and a compd. contg. reactive H, in which the compd. contg. reactive H is dispersed in a nonreactive matrix, which mixt. is not or low reactive at ambient conditions and highly reactive under selected

conditions, is applied onto a substrate at ambient temp., followed by heating. At ambient temp. the compd. contg. reactive H is a solid material, a powder, a granule, a flake or grind or a ground mixt. The coatings, coated substrates, adhesives, films, sheets, impregnated substrates, synthetic leathers, in-mold coatings, coated leathers, coated poly(vinyl chloride), coated nonwovens, coated coagulated polyurethane substrates, breathable coated substrates, are obtained by applying the the title process.

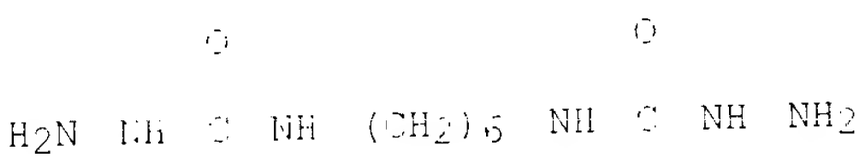
IT **332421-29-1P 332421-30-4P**
PL: IMF (Industrial manufacture); PRP (Properties); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(coating or film; for coating, adhesive, a film or sheet formulated from a reactive mixt. of long pot life, fast reaction, and low toxic vapors)

RN 332421-29-1 HCAPLUS

CN Hexanedioic acid, polymer with 2,2-dimethyl-1,3-propanediol, 2-ethyl-2-(hydroxymethyl)-1,3-propanediol, 1,6-hexanediol, N,N'-1,6-hexanediylbis[hydrazinecarboxamide] and 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethylcyclohexane (9CI) (CA INDEX NAME)

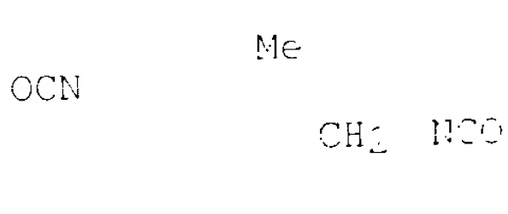
CM 1

CRN 51410-70-1
CMF C9 H20 N6 O2



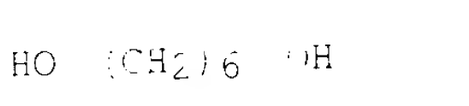
CM 2

CRN 4098-71-9
CMF C12 H16 N2 O2



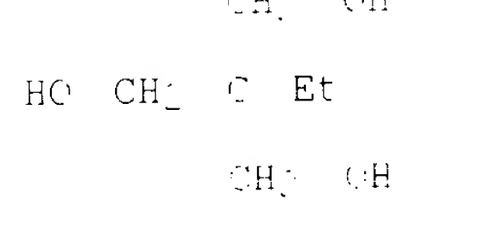
CM 3

CRN 629-11-5
CMF C6 H14 O2



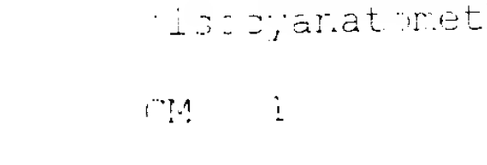
CM 4

CRN 126-30-7
CMF C5 H12 O2



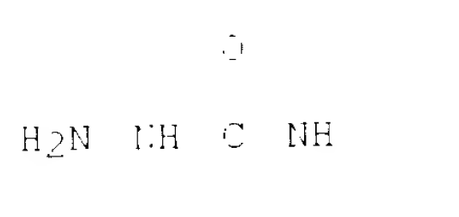
CM 5

CRN 124-04-9
CMF C6 H10 O4



CM 6

CRN 77-99-6
CMF C6 H14 O3



RN 330421-30-4 HCAPLUS
CN Hexanedioic acid, polymer with 2,2-dimethyl-1,3-propanediol, 2-ethyl-2-(hydroxymethyl)-1,3-propanediol, 1,6-hexanediol, N-[3-[[(hydrazinocarbonyl)amino]methyl]-3,5,5-trimethylcyclohexyl]hydrazinecarboxamide and 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethylcyclohexane (9CI) (CA INDEX NAME)

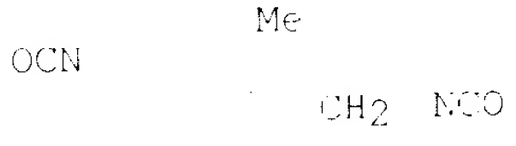
CM 1

CRN 52284-45-4
CMF C12 H26 N6 O2



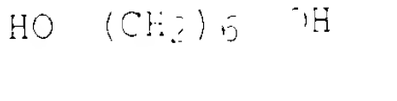
CM 2

CRN 4098-71-9
CMF C15 H18 N2 O2



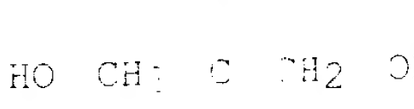
CM 3

CRN 629-11-8
CMF C6 H14 O2



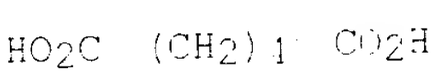
CM 4

CRN 126-30-7
CMF C5 H12 O2



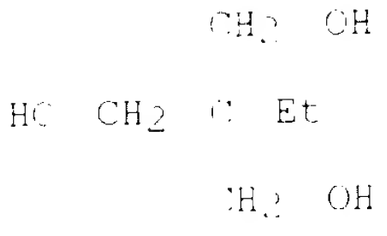
CM 5

CRN 124-04-9
CMF C6 H10 O4

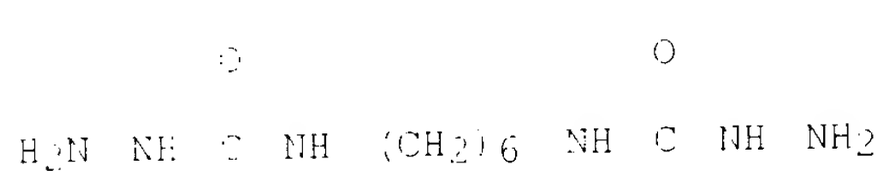


CM 6

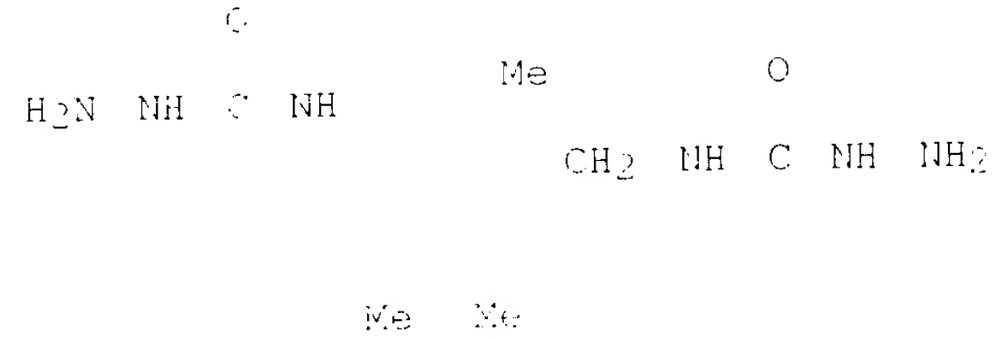
CRN 77-99-6
CMF C6 H14 O3



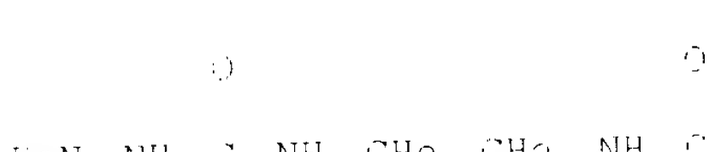
IT **51440-70-1P 52284-45-4P**
PL: IMF (Industrial manufacture); FCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(curative; for coating, adhesive, a film or sheet formulated from a reactive mixt. of long pot life, fast reaction, and low toxic vapors)
RN 51440-70-1 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,6-hexanediylbis- (9CI) (CA INDEX NAME)



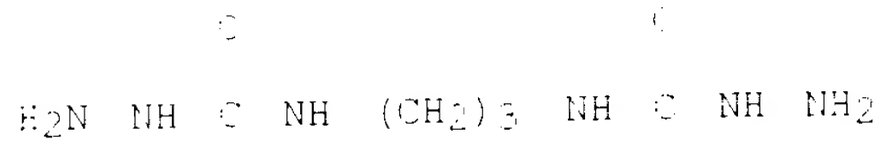
RN 52284-45-4 HCAPLUS
CN Hydrazinecarboxamide, N-[3-[[(hydrazinocarbonyl)amino]methyl]-3,5,5-trimethylcyclohexyl]- (9CI) (CA INDEX NAME)



IT **32251-26-6 126953-51-3 332421-34-8**
PL: TEM (Technical or engineered material use); USES (Uses)
(curative; for coating, adhesive, a film or sheet formulated from a reactive mixt. of long pot life, fast reaction, and low toxic vapors)
RN 32251-26-6 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)



RN 126953-51-3 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,3-propanediylbis- (9CI) (CA INDEX NAME)



RN 332421-34-8 HCAPLUS

CN Hydrazinecarboxamide, N,N'-1,4-butanediylbis- (9CI) (CA INDEX NAME)

L9 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:167451 HCAPLUS
DOCUMENT NUMBER: 134:198060
TITLE: Radiopharmaceutical products and their preparation procedure
INVENTOR(S): Bellande, Emmanuel; Jallet, Pierre; Tenibot, Benoit
PATENT ASSIGNEE(S): Cis Bio International, Fr.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001015746 | A1 | 20010308 | WO 2000-IB1161 | 20000823 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| FR 2797769 | A1 | 20010302 | FR 1999-10970 | 19990901 |
| BR 2000013729 | A | 20020507 | BR 2000-13729 | 20000823 |
| EP 1210137 | A1 | 20020605 | EP 2000-951784 | 20000823 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | |
| JP 2003508499 | T2 | 20030304 | JP 2001-520157 | 20000823 |
| EE 200200105 | A | 20030415 | EE 2002-105 | 20000823 |
| BG 106438 | A | 20020930 | BG 2002-106438 | 20020226 |
| NO 20020901001 | A | 20020411 | NO 2002-1001 | 20020226 |
| | | | FR 1999-10970 A | 19990901 |
| | | | WO 2000-IB1161 W | 20000823 |

PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 134:198060

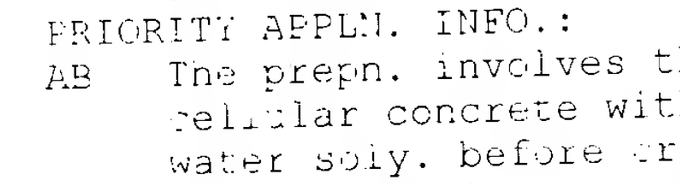
AB The present invention relates to radiopharmaceutical products and their prepn. procedure. These products can be used for pulmonary scintigraphy or for therapy. They comprise a polysaccharide and sequestering groups of formulas R-NH-, R-N=, and R-N(R')-N= in which R is a hydrocarbon or arom. group comprising at least one atom of sulfur, and R' is an atom of hydrogen or an alkyl grouping such as Me, said sequestering groups forming a chelate type complex with a radioactive metal such as technetium.

IT **3766-55-0DP**, 4-Allyl 3-thiosemicarbazide, radiolabeled reaction product with oxidized starch **6610-29-3DP**, 4-Methyl 3-thiosemicarbazide, radiolabeled reaction product with oxidized starch RL: BPR (Biological process); BSU (Biological study, unclassified); GPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(radiopharmaceutical kits for scintigraphy)

RN 3766-55-0 HCAPLUS
CN Hydrazinecarbothioamide, N-2-propenyl- (9CI) (CA INDEX NAME)

RN 6610-29-2 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

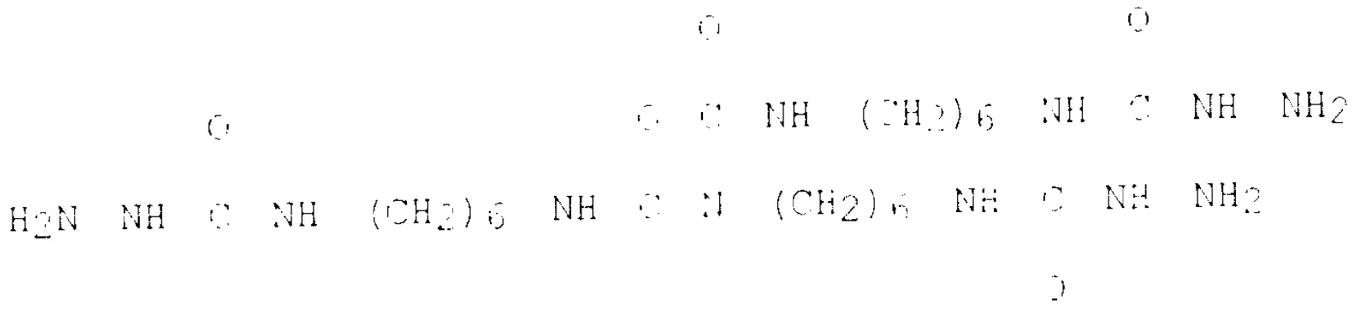
L9 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:114047 HCAPLUS
DOCUMENT NUMBER: 130:200010
TITLE: Lightweight cellular concrete having waterproof coatings and its preparation
INVENTOR(S): Ito, Yasuyuki; Watanabe, Tomoiya; Nakanishi, Masuhiko
PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 11043385 | A2 | 19990216 | JP 1997-198765 | 19970724 |
| PRIORITY APPLN. INFO.: | | | JP 1997-198765 | 19970724 |

AB The prepn. involves the following steps; (1) impregnating lightweight cellular concrete with an aq. soln. contg. a hardenable resin which shows water soly. before cross linking, (2) **crosslinking** the resin, and (3) forming a coating on the surface. The aq. soln. may contain a hardening agent. The resulting concrete products are also claimed.

IT **175870-12-9P**
RL: IMF (Industrial manufacture); MOA (Modifier or additive use); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**crosslinking** agent; prepn. of lightweight cellular concrete having **crosslinked** polymer layers and waterproofing coating layers)

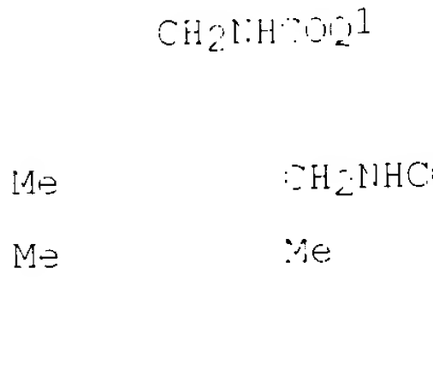
RN 175870-12-9 HCAPLUS
CN 2,9,11,13,20-Pentaazaheneicosanedioic acid, 11-[6-[(hydrazinocarbonyl)amino]hexyl]-10,12-dioxo-, dihydrazide (9CI) (CA INDEX NAME)



L9 ANSWER 7 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:724187 HCAPLUS
DOCUMENT NUMBER: 130:14992
TITLE: Isophoronebis(semicarbazides), their preparation, their semicarbazones, and room-temperature-curable water-resistant coating compositions with good storage stability containing them
INVENTOR(S): Yokota, Masahisa; Miyazaki, Takayuki; Ueyanagi, Kaoru
PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 10298158 | A2 | 19981110 | JP 1997-120103 | 19970424 |
| PRIORITY APPLN. INFO.: | | | JP 1997-120103 | 19970424 |
| OTHER SOURCE(S): | | MARPAT 130:14992 | | |

GI

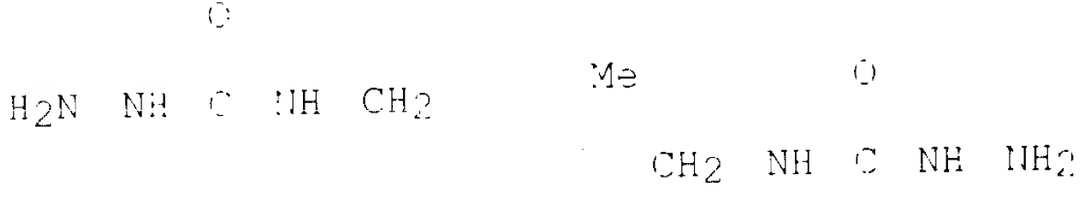


AB The semicarbazides I [Q1, Q2 = NR3NH2 (R3 = H, C1-20 alkyl, alicyclic group, aryl), NHNR3R4NR3NH2 (R4 = linear or branched C2-20 alkylene, C5-20 cycloalkylene, C6-10 arylene which may be substituted with C1-8 alkyl or alkoxy), NHNR3COR4CONR3NH2, NHNR3CO(NHNH)xCONHNH2 (x = 1-5), NHNR3CONHR4NHCONR3NH2] are prepd. by treatment of isophorone diisocyanate and hydrazines. Semicarbazones are prepd. by treatment of I with R1R2CO [R1, R2 = H, linear or branched C2-20 aliph. group, C5-20 alicyclic group, (un)substituted aryl; R1 and R2 may be bonded to each other forming a ring]. The coating compns. contain (A) I, and/or (B) the above semicarbazones, and (C) polycarbonyl compds. at (C)/[(A)+(B)] = 99.9:0.1-10/90. The compns. provide coating having high hardness and good waterproofness. An aq. emulsion contained methacrylic acid-Me methacrylate-Bu acrylate-diacetone acrylamide copolymer and isophorone bis(semicarbazide).

IT **216143-35-0P**
RL: IMF (Industrial manufacture); MOA (Modifier or additive use); RCT

(Reactant); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of isophoronebis(semicarbazides) as **crosslinking** agents for room-temp.-curable coating compns. for high hardness and good waterproofness)

RN 216143-35-0 HCAPLUS
CN Hydrazinecarboxamide, N,N'-[(1,5,5-trimethyl-1,3-cyclohexanediyl)bis(methylene)]bis- (9CI) (CA INDEX NAME)



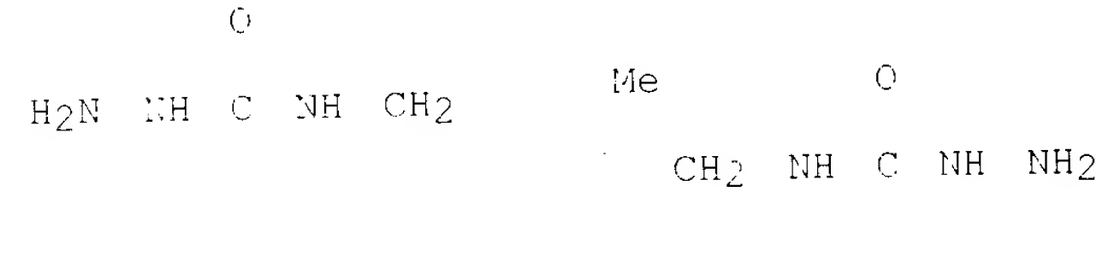
Me Me

IT **216143-36-1P**
PL: IMF (Industrial manufacture); PRP (Properties); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(prepn. of isophoronebis(semicarbazides) as **crosslinking** agents for room-temp.-curable coating compns. for high hardness and good waterproofness)

RN 216143-36-1 HCAPLUS
CN 2-Propenoic acid, 2-methyl-, polymer with butyl 2-propenoate, N-(1,1-dimethyl-3-oxobutyl)-2-propenamide, methyl 2-methyl-2-propenoate and N,N'-[(1,5,5-trimethyl-1,3-cyclohexanediyl)bis(methylene)]bis[hydrazinecarboxamide] (9CI) (CA INDEX NAME)

CM 1

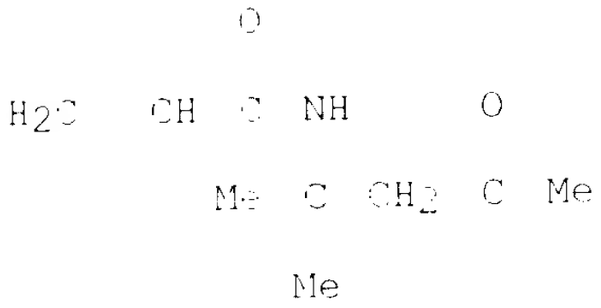
CRN 216143-35-0
MF C18 H32 N6 O2



Me Me

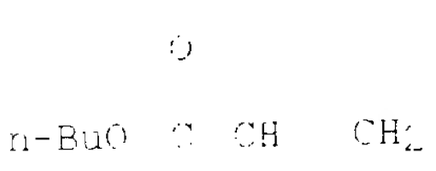
CM 2

CRN 2873-97-4
CMF C9 H15 N O2



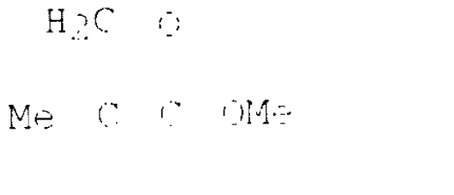
CM 3

CRN 141-32-2
CMF C7 H12 O2



CM 4

CRN 80-62-6
CMF C5 H8 O2



CM 5

CRN 79-41-4
CMF C4 H6 O2

L9 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:112262 HCAPLUS
DOCUMENT NUMBER: 128:196654
TITLE: Polypeptides having a single covalently bound N-terminal water-soluble polymer
INVENTOR(S): Wei, Ziping; Menon-rudolph, Sunitha; Ghosh-Dastidar, Pradip
PATENT ASSIGNEE(S): Ortho Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9830609 | A2 | 19980716 | WO 1997-US13756 | 19970801 |
| WO 9830609 | A3 | 19981105 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BF, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | |
|---|---|---|---|---|
| AU 9738055 | A1 | 19980225 | AU 1997-38055 | 19970801 |
| EP 917589 | A | 19990519 | BR 1997-11009 | 19970801 |
| CN 1226176 | A | 19990818 | CN 1997-196529 | 19970801 |
| EP 964702 | A2 | 19991222 | EP 1997-936407 | 19970801 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI

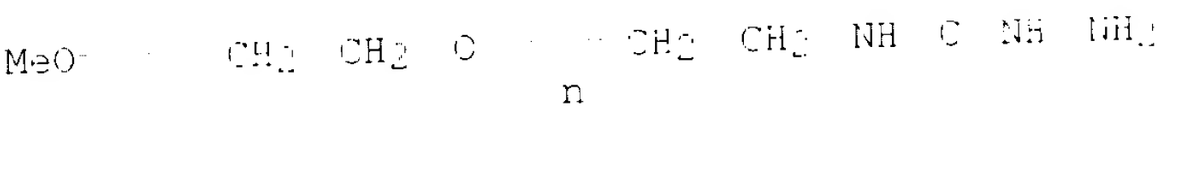
| | | | |
|---|---|---|---|
| NZ 333993 | A | 20000218 | NZ 1997-333993 | 19970801 |
| JP 2000515553 | T2 | 20001121 | JP 1998-508179 | 19970801 |
| RU 2199547 | C2 | 20030227 | RU 1999-103679 | 19970801 |
| NO 9900365 | A | 19990319 | NO 1999-365 | 19990127 |
| MX 9901144 | A | 20010301 | MX 1999-1144 | 19990201 |
| | | | US 1996-30351P | P 19960802 |
| | | | WO 1997-US13756 | W 19970801 |

PRIORITY APPLN. INFO.:

AB This invention provides comprs. consisting essentially of a polypeptide such as erythropoietin and a water-sol. polymer such as PEG covalently bound thereto at the N-terminal .alpha.-carbon atom via a hydrazone or reduced hydrazone bond, or an oxime or reduced oxime bond. This invention also provides methods of making the instant comprs., pharmaceutical comprs. comprising same, and kits for use in prepg. same.

IT **167394-62-9**
PL: BCT (Reactant); RACT (Reactant or reagent)
(polypeptides having a single covalently bound N-terminal water-sol. polymer)

RN 167394-62-9 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[(hydrazinocarbonyl)amino]ethyl]-.omega.-methoxy- (9CI) (CA INDEX NAME)




L9 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:340480 HCAPLUS
DOCUMENT NUMBER: 127:3745
TITLE: Reagent for the detection and isolation of carbohydrates or glycan receptors
INVENTOR(S): Watzele, Manfred; Fernholz, Erhard; Von Der Eltz, Herbert
PATENT ASSIGNEE(S): Boehringer Mannheim Gmbh, Germany
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 749490 | A1 | 19970423 | EP 1996-116773 | 19961018 |
| EP 749490 | B1 | 20011219 | | |
| R: DE, ES, FR, GB, IT | | | | |
| DE 19539008 | A1 | 19970424 | DE 1995-19539008 | 19951019 |
| US 6136546 | B1 | 20010417 | US 1996-738736 | 19961018 |
| JP 09176106 | A2 | 19970708 | JP 1996-277834 | 19961021 |

PRIORITY APPLN. INFO.: DE 1995-19539008 A 19951019
OTHER SOURCE(S): MARPAT 127:2745

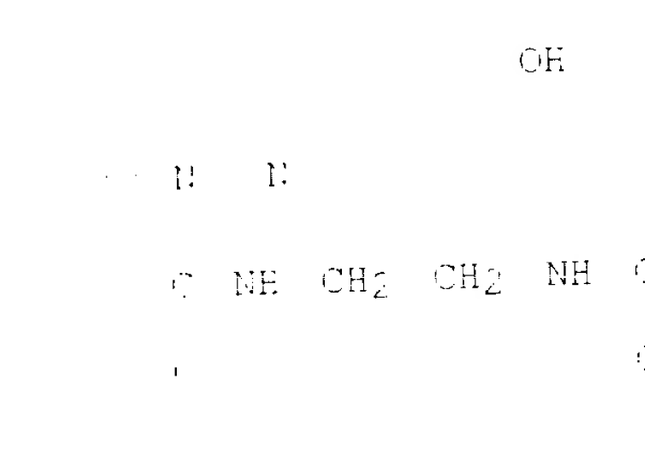
AB The finding concerns compds., which contain a chromophore and a ligand (e.g., biotin or a biotin deriv.) that can bind to streptavidin and/or avidin, that are suitable for binding to mols. that contain an aldehyde, ketone, hemiacetal, and/or hemiketal function. The finding also concerns **conjugates** formed from these compds. as well as a method for detecting or isolating carbohydrates or glycan receptors by using such **conjugates**.

IT **190126-38-6P**
PL: ARG (Analytical reagent use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(reagent for detecting and isolating carbohydrates or glycan receptors)

RN 190126-38-6 HCAPLUS
CN Hydrazinecarboxamide, N-[2-[[2-[(4-hydroxyphenyl)azo]benzoyl]amino]ethyl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

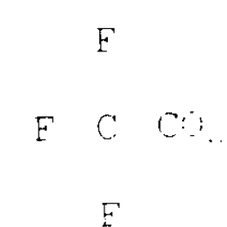
CM 1

CRN 190126-37-5
CMF C16 H18 N6 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L9 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:[illegible] HCAPLUS
DOCUMENT NUMBER: 126:2[illegible]
TITLE: Di- and triaminoguanidines, and methods of use
INVENTOR(S): Wagle, Dilip R.; Ulrich, Peter C.; Bernat, Anthony
PATENT ASSIGNEE(S): Altech Inc., USA; Rockefeller University
SOURCE: U.S., 13 pp., Cont.-in-part of U.S. Ser. No. 274,243, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English.
FAMILY ACC. NUM. COUNT: 33
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5612332 | A | 19970318 | US 1995-487069 | 19950607 |
| EP 382402 | A2 | 19900822 | EP 1989-102406 | 19890213 |
| EP 382402 | A3 | 19910925 | | |
| EP 382402 | B1 | 19971124 | | |
| R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE | | | | |
| AT 97741 | E | 19971215 | AT 1989-102406 | 19890213 |
| US 5140048 | A | 19920818 | US 1990-519664 | 19900507 |
| US 5126442 | A | 19920630 | US 1991-699755 | 19910514 |
| US 5254593 | A | 19931019 | US 1991-[illegible] | 19911[illegible] |
| JP 05178813 | A2 | 19930713 | JP 1991-[illegible] | 19911[illegible] |
| US 5356895 | A | 19941018 | US 1992-889141 | 19920527 |
| WO 9313775 | A1 | 19930722 | WO 1993-US376 | 19930115 |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9335840 | A1 | 19930803 | AU 1993-35840 | 19930115 |
| US 5811075 | A | 19980922 | US 1995-487398 | 19950607 |
| WO 9640663 | A1 | 19961219 | WO 1996-US9376 | 19960607 |
| W: AU, CA, IL, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9661366 | A1 | 19961230 | AU 1996-61366 | 19960607 |
| US 5852009 | A | 19981222 | US 1997-784861 | 19970116 |
| US 6114323 | A | 20000905 | US 1998-215612 | 19981217 |
| US 2002115724 | A1 | 20020822 | US 2001-954514 | 20010917 |

PRIORITY APPLN. INFO.:

US 1984-590810 A2 19840319
US 1985-788032 A1 19851114
US 1987-119958 A2 19871113
US 1988-264930 A2 19881102
US 1990-605654 A3 19901030
US 1992-889141 A3 19920527
US 1994-274243 B2 19940713
EP 1989-102406 A 19890213
US 1995-487069 B2 19950607
US 1997-784861 A3 19970116
US 1998-[illegible] A3 19981[illegible]
US 1999-[illegible] A3 19990[illegible]
US 1999-[illegible] B1 19991[illegible]
US 1999-[illegible] A2 19991[illegible]
US 1999-[illegible] A3 19991[illegible]
US 1999-[illegible] B1 19991[illegible]
US 2001-[illegible] A [illegible]
US 2001-[illegible] B1 20010[illegible]
WO 1993-US376 A 19930115
US 1993-161840 B1 19931203
US 1994-[illegible] B1 19940[illegible]
US 1995-487199 A 19950607

WO 1996-US9376 W 19960607
US 1997-764861 A1 19970116
US 1998-215612 A1 19981217
US 2000-561541 A3 20000423

OTHER SOURCE(S): MARPAT 126:182832

AB The present invention relates to compns., compns. and methods for inhibiting nonenzymic **crosslinking** (protein aging). Accordingly, a compn. is disclosed which comprises a di- or tri-aminoguanidine capable of inhibiting the formation of advanced glycosylation end products of target proteins. The method comprises contacting the target protein with the compn. Both industrial and therapeutic applications for the invention are envisioned, as food spoilage and animal protein aging can be treated.

IT **13431-34-0**, 4-Ethyl-3-thiosemicarbazide
RL: RCT (Reactant); RACT (Reactant or reagent)
(di- and triaminoguanidines and methods of use to prevent protein aging)

RN 13431-34-0 HCAPLUS
CN Hydrazinecarbothioamide, N-ethyl- (9CI) (CA INDEX NAME)

?

E NH2 C NH NH2

L9 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:127504 HCAPLUS
DOCUMENT NUMBER: 126:129000
TITLE: Semicarbazide-containing linker compounds for formation of stably-linked **conjugates** and methods related thereto
INVENTOR(S): Berninger, Ronald W.; Ledge, Mark S.; Tarnowski, Stanley Joseph, Jr.
PATENT ASSIGNEE(S): Cellpro, Incorporated, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9640263 | A2 | 19961219 | WO 1996-US8983 | 19960604 |
| WO 9640263 | A3 | 19970417 | | |
| W: JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5856371 | A | 19990105 | US 1995-486980 | 19950607 |
| | | | US 1995-486989 | 19950607 |

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 126:129000

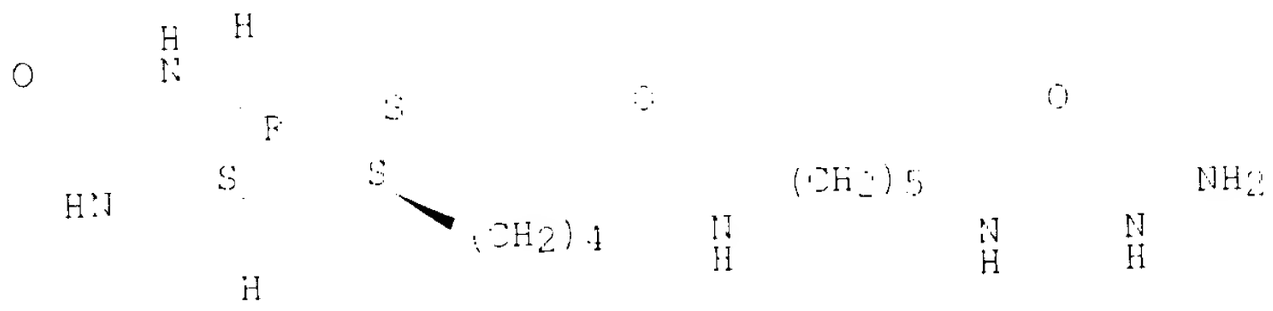
AB Linker compds. for formation of stably-linked **conjugates** are disclosed. Such linker compds. are semicarbazide-contg. linker compds. useful in forming **conjugates** having stable semicarbazone linkages. The stably-linked **conjugates** have utility in a variety of immunodiagnostic and sepn. techniques.

IT **186422-63-9P**
RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(semicarbazide-contg. linker compds. for formation of stably-linked **conjugates** and methods related thereto)

RN 186422-63-9 HCAPLUS
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[5-[(hydrazinocarbonyl)amino]pentyl]hexahydro-2-oxo-, [3aS-(3a.alpha.,4.beta.,6a.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



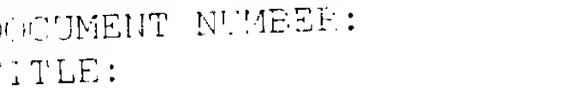
L9 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:9948 HCAPLUS
DOCUMENT NUMBER: 126:128771
TITLE: Substituted thioureas as **bifunctional** chelators, their preparation, **conjugates** with peptides, proteins, and antibodies, and their use in imaging of tumors and thrombi
INVENTOR(S): Coughlin, Daniel J.; Belinka, Jr Benjamin A.
PATENT ASSIGNEE(S): Cytogen Corporation, USA
SOURCE: U.S., 32 pp., Cont.-in-part of U.S. 5,326,856.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

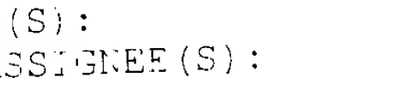
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5565468 | A | 19961217 | US 1994-204197 | 19940627 |
| US 5326856 | A | 19940705 | US 1992-866375 | 19920409 |
| WO 9321151 | A1 | 19931028 | WO 1993-US3208 | 19930408 |

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1992-866375 19920409
WO 1993-US3208 19930408

OTHER SOURCE(S): MARPAT 126:128771
GI





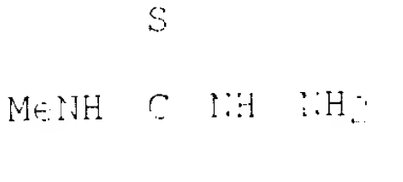
I

AB Chelating agents useful for coupling metal ions to biol. active mols. are disclosed. In particular, substantial thioureas for chelating metals, e.g. technetium, are provided that can be **conjugated** to a

targeting mol. such as an antibody, a peptide or a protein. Prepn. of the chelating agents of the invention, e.g. I, is described, as are **conjugation** to an antibody and to a peptide and use of the **conjugates** in tumor imaging and thrombus imaging.

IT **6610-29-3**, 4-Methyl-3-thiosemicarbazide
RL: PCT (Reactant); RACT (Reactant or reagent)
(reaction; substituted thioureas as **bifunctional** chelators, prepn., **conjugates** with peptides, proteins, and antibodies, and use in imaging of tumors and thrombi)

RN 6610-29-3 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)



MeNH C NH NH2

L9 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:741867 HCAPLUS
DOCUMENT NUMBER: 126:42121
TITLE: Method of photochemical **immobilization** of ligands using quinones
INVENTOR(S): Jacobsen, Mogens Havsteen; Koch, Troels
PATENT ASSIGNEE(S): Jacobsen, Mogens, Havsteen, Ben.
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9631547 | A1 | 19961010 | WO 1996-DK167 | 19960403 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| CA 2211053 | AA | 19961010 | CA 1996-2211053 | 19960403 |
| AU 9653829 | A1 | 19961023 | AU 1996-53829 | 19960403 |
| AU 699321 | B2 | 19981203 | | |
| EP 820483 | A1 | 19980128 | EP 1996-909990 | 19960403 |
| EP 820483 | B1 | 20001213 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI | | | | |
| JP 11505554 | T2 | 19990521 | JP 1996-530895 | 19960403 |
| JP 3124037 | B2 | 20010115 | | |
| AT 198079 | E | 20001215 | AT 1996-909990 | 19960403 |
| ES 2153097 | T3 | 20010216 | ES 1996-909990 | 19960403 |
| US 6033784 | A | 20000307 | US 1997-930623 | 19971007 |
| PRIORITY APPLN. INFO.: | | | DK 1995-425 A | 19950407 |
| | | | WO 1996-DK167 W | 19960403 |

OTHER SOURCE(S): CASREACT 126:42121; MARPAT 126:42121

AB A method is disclosed for **immobilizing** a ligand on the surface of a carbon-contg. substrate material, said method comprising a photochem. step of linking .gtoreq.1 photochem. reactive cmpds. to a carbon-contg.

material surface, wherein the photochem. reactive compd. is a quinone compd. contg. a cyclic hydrocarbon or 2-10 fused cyclic hydrocarbons, with at least 2 **conjugated** carbonyl groups, and wherein the photochem. step comprises irradn. of the photochem. reactive compd. with nonionizing electromagnetic radiation having a wavelength in the range from UV to visible light. The products of this invention can be used as, e.g., carriers for solid-phase immunoassays.

IT **172422-03-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(photochem. **immobilization** of ligands using quinones)

RN 172422-03-6 HCAPLUS
CN 2-Anthracenecarboxamide, N-[3-[(hydrazinothioxomethyl)amino]propyl]-9,10-dihydro-9,10-dioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:319761 HCAPLUS
DOCUMENT NUMBER: 123:89553
TITLE: PEG hydrazone and PEG oxime linkage forming reagents and protein derivatives.
INVENTOR(S): Wright, David E.
PATENT ASSIGNEE(S): Ortho Pharmaceutical Corp., USA
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 605963 | A2 | 19940713 | EP 1993-309835 | 19931207 |
| EP 605963 | A3 | 19951108 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| CA 2110543 | AA | 19940610 | CA 1993-2110543 | 19931202 |
| FI 9305495 | A | 19940610 | FI 1993-5495 | 19931208 |
| NO 9304477 | A | 19940610 | NO 1993-4477 | 19931208 |
| ZA 9309214 | A | 19950608 | ZA 1993-9214 | 19931208 |
| AU 9352393 | A1 | 19940623 | AU 1993-52393 | 19931209 |
| JP 07196625 | A2 | 19950801 | JP 1993-340709 | 19931209 |
| | | | US 1992-987739 | 19921209 |
| | | | US 1993-45052 | 19930407 |
| | | | US 1993-157343 | 19931123 |

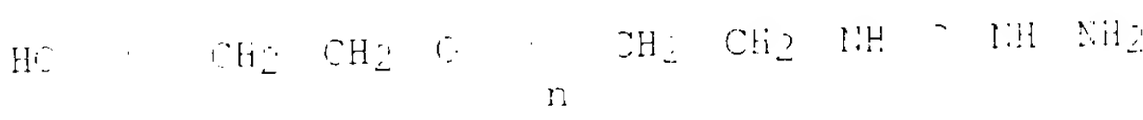
PRIORITY APPLN. INFO.:

AB Compns. for modifying polypeptides with PEG or other water-sol. org. polymers are described. The water-sol. polymer reagents include hydrazine, hydrazine carboxylate, semicarbazole, thiosemicarbazide, carbonic acid dihydrazide, carbazide, thiocarbazide, and arylhydrazide derivs. as well as oxylamine derivs. of water-sol. org. polymers, such as

polyethylene glycol, polypropylene glycol, polyoxyethylated polyol, heparin, heparin fragments, dextran polysaccharides, polyamino acids, and polyvinyl alc. Kits for modifying polypeptides with the above water-sol. polymer reagents are also provided. Thus, erythropoietin was modified by oxidn. and treatment with monomethoxypolyoxyethylene semicarbazide and the product was sepd. by chromatog. The antigenicity and the effect on hematocrit levels of the above derivs. were demonstrated.

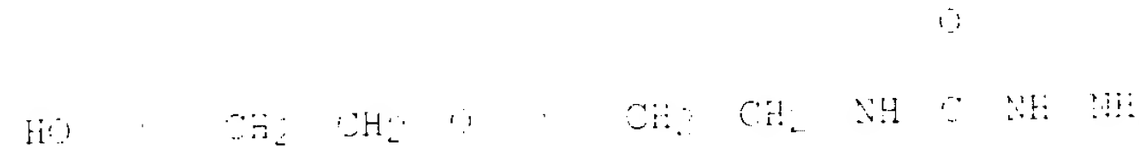
IT **160556-27-4DP**, reaction products with protein derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified.; SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and biol. activity of polyoxyethylene-coupled protein derivs.)

RN 160556-27-4 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[(hydrazinocarbonyl)amino]ethyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

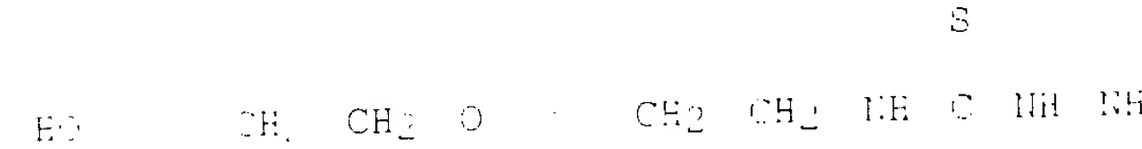


IT **160556-27-4P 160556-28-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and biol. activity of polyoxyethylene-coupled protein derivs.)

RN 160556-27-4 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[(hydrazinocarbonyl)amino]ethyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 160556-28-5 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[(hydrazinothioxomethyl)amino]ethyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



L9 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:95783 HCAPLUS
DOCUMENT NUMBER: 120:95783
TITLE: Inhibitors of thrombosis
INVENTOR(S): Wasuk, Georg Phillip; Webb, Thomas Roy; Pearson, Daniel Andrew
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9317706 | A1 | 19930819 | WO 1993-US1307 | 19930212 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 627439 | A1 | 19941214 | EP 1993-905930 | 19930212 |
| EP 627439 | B1 | 19980930 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 07503961 | T2 | 19950427 | JP 1993-514315 | 19930212 |
| JP 3194963 | B2 | 20010806 | | |
| AT 171709 | E | 19981015 | AT 1993-905930 | 19930212 |
| CA 2129339 | C | 20020910 | CA 1993-2129339 | 19930212 |

PRIORITY APPLN. INFO.: US 1992-836123 A 19920214
WO 1993-US1307 W 19930212

OTHER SOURCE(S): MARPAT 120:95783

AB Peptide aldehyde analogs, AcR-AA-L-Pro-Arg-al (AcR = hydrophobic acyl group; AA = Glu, Asp, or equiv.), inhibit thrombin or Factor Xa and are thus useful for preventing or treating conditions in mammals characterized by abnormal thrombosis. N-(3-phenylpropanyl)-L-Asp-L-Pro-L-argininal (prepn. given) inhibited thrombin, Factor Xa, and plasmin with IC50 values of 234, 91.5, and 326 nM, resp., and showed antithrombotic activity in a rat model.

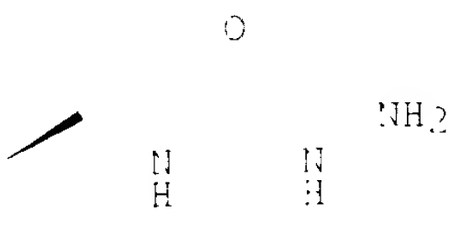
IT **139976-29-7P 151275-26-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); FACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of antithrombotic peptide aldehyde analog)

RN 139976-29-7 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-[[(hydrazinocarbonyl)amino]methyl]-, trans-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

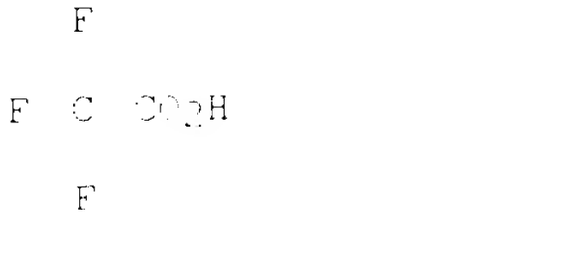
CRN 139976-28-6
CMF C9 H17 N3 O3

Relative stereochemistry.



CM 2

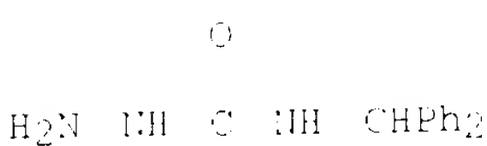
CRN 76-05-1
CMF C2 H F3 O2



RN 111275-26-2 HCAPLUS
CN Hydrazinecarboxamide, N-(diphenylmethyl)-, mono(trifluoroacetate) (9CI)
(CA INDEX NAME)

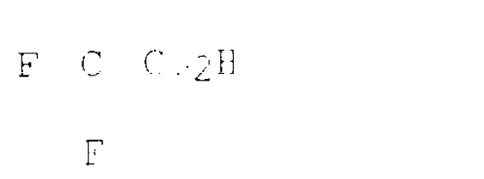
CM 1

CRN 150908-39-7
CMF C14 H15 N3 O



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L9 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:49591 HCAPLUS
DOCUMENT NUMBER: 120:49591
TITLE: Substituted thioureas as **bifunctional** chelators for **conjugation** to antibodies or other biological targeting molecules
INVENTOR(S): Coughlin, Daniel J.; Belinka, Benjamin A., Jr.
PATENT ASSIGNEE(S): Cytogen Corp., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9321151 | A1 | 19931028 | WO 1993-US3208 | 19930408 |
| W: CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5326856 | A | 19940705 | US 1992-866375 | 19920409 |
| EP 635001 | A1 | 19950125 | EP 1993-911594 | 19930408 |

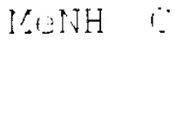
EP 63[illegible]01 B1 19970820
B: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 0[illegible]240 T2 19960910 JP 1993-518423 19930408
AT 1[illegible]4 E 19971015 AT 1993-911594 19930408
ES 2[illegible]95 T3 19980116 ES 1993-911594 19930408
US 5[illegible]468 A 19941227 US 1994-204197 19940302
US 5[illegible]885 A 19960618 US 1994-268445 19940630
PRIORITY APPLN. INFO.: US 1992-866371 19920410
WO 1993-US3208 19930408

OTHER SOURCE(S): MARPAT 120:49591

AB The title chelating agents are LD[NHC(:S)NHR]L [L = linker; D = (cyclo)alkyl, aryl; R = H, (NH)a(CH2)b(C:Y)c(NH)d(CH2)eZ (a = 0, 1; b, e = 0-10; c = 0, 1 (if c = 1, Y = S, O, H2); d = 0-2; Z = H, SO3H, CO2H,, OH, H2PO3, N+(R')3X- (R' = C1-4 alkyl; X- = counterion, such as halide or acid anion))]; the chelating agents are useful for coupling metal ions to biol. active mols. (antibodies, peptides, etc.). Prepn. of several chelating agents of the invention is described. Thus, 3,5-di-(1-trimethylammoniumacetyl)-4-thiosemicarbazidobenzoic acid dichloride salt (I) was prepd. from 3,5-diisothiocyanatobenzoic acid (prepn. given) and (carboxymethyl)trimethylammonium chloride hydrazide. I was **conjugated** to a peptide (CYRGDVRGDF-NH2), and the **conjugate** was labeled with 99mTc. The labeled peptide **conjugate** was used in the imaging of thrombi in rabbits. Prepn. and use in tumor imaging of a labeled antibody **conjugate** is also described.

IT **6610-29-3**, 4-Methyl-3-thiosemicarbazide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in **bifunctional** substituted thiourea chelating agent prepn.)

RN 6610-29-3 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)



MeNH C NH NH2

L9 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:617414 HCAPLUS
DOCUMENT NUMBER: 119:217414
TITLE: Peptide aldehyde analogs for trypsin inhibitors
INVENTOR(S): Bruncko, Terence Kevin; Pepe, Michael Gary; Pearson, Daniel Andrew; Webb, Thomas Roy
PATENT ASSIGNEE(S): Corvas International, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9314779 | A1 | 19930805 | WO 1993-US966 | 19930129 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 6[illegible]925 | A1 | 19941214 | EP 1993-905778 | 19930129 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |

| | | | | |
|---|---|---|---|---|
| JP 07503715 | T2 | 19950420 | JP 1993-513488 | 19930129 |
| US 5534498 | A | 19960709 | US 1993-11666 | 19930129 |
| PRIORITY APPLN. INFO.: | | | US 1992-828388 | 19920130 |
| | | | US 1993-11666 | 19930129 |
| | | | WO 1993-US906 | 19930129 |

OTHER SOURCE(S): MARPAT 119:217414

AB Peptide aldehyde analogs are disclosed which have substantial potency and specificity as innibitors of mammalian pancreatic trypsin. The compds. of the invention are useful in the prevention and treatment of tissue damage or destruction assocd. with pancreatitis. Prepn. of the analogs is described. Thus, N-t-butoxycarbonyl-L-Asp-L-Pro-L-argininal (I) (prepn. given; nad a Ki against trypsin of 0.00045 .mu.M. The effectiveness of I in an animal model for pancreatitis was also demonstrated.

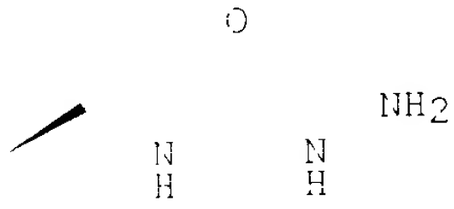
IT **139976-29-7P 150908-39-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in peptide aldehyde analog prepn. for trypsin inhibitor)

RN 139976-29-7 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-[[(hydrazinocarbonyl)amino]methyl]-, trans-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

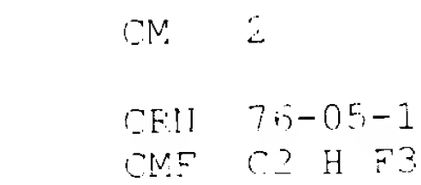
CRN 139976-28-6
CMF C9 H17 N3 O3

Relative stereochemistry.

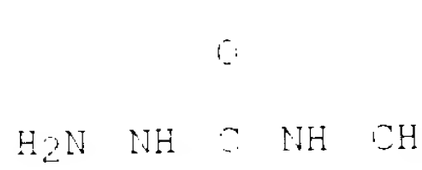


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 150908-39-7 HCAPLUS
CN Hydrazinecarboxamide, N-(diphenylmethyl)- (9CI) (CA INDEX NAME)

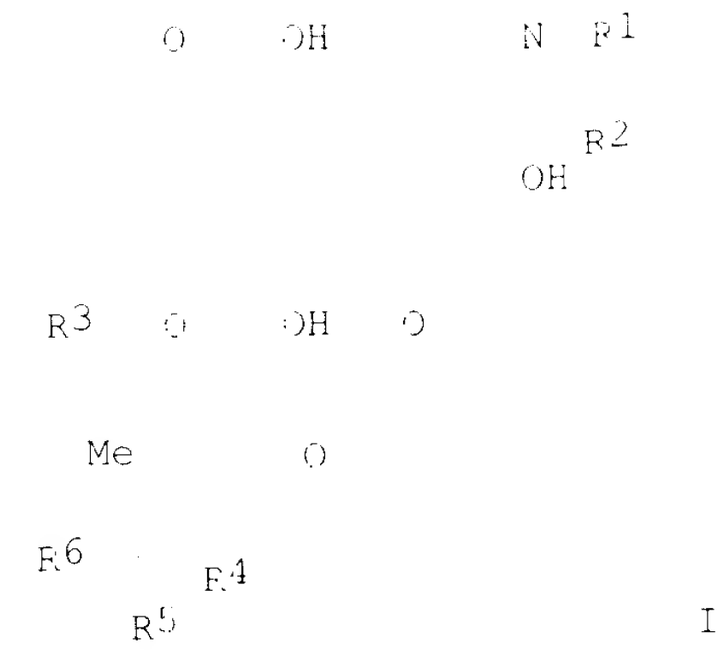


L9 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:214841 HCAPLUS
DOCUMENT NUMBER: 116:214841
TITLE: Preparation of anthracycline **immunoconjugates** as neoplasm inhibitors
INVENTOR(S): Kaneko, Takushi; Willner, David; Monkovic, Ivo; Greenfield, Robert S.; Braslawsky, Gary R.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 457550 | A2 | 19911121 | EP 1991-107737 | 19910513 |
| EP 457550 | A3 | 19920701 | | |
| EP 457550 | B1 | 19990714 | | |
| F: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| US 5137877 | A | 19920811 | US 1990-522996 | 19900514 |
| US 5137877 | B1 | 19960130 | | |
| AU 9174038 | A1 | 19911114 | AU 1991-74038 | 19910403 |
| AU 646850 | B2 | 19940310 | | |
| FI 9102285 | A | 19911115 | FI 1991-2285 | 19910510 |
| JP 04356765 | A2 | 19921209 | JP 1991-199757 | 19910510 |
| JP 3010319 | B2 | 20000221 | | |
| ZA 9103591 | A | 19920226 | ZA 1991-3591 | 19910513 |
| AT 182141 | E | 19990715 | AT 1991-107737 | 19910513 |
| ES 2134761 | T3 | 19991016 | ES 1991-107737 | 19910513 |
| CA 2042503 | AA | 19911115 | CA 1991-2042503 | 19910514 |
| CA 2042503 | C | 20020723 | | |
| US 5340566 | A | 19940823 | US 1992-865062 | 19920408 |
| JP 2000026404 | A2 | 20000125 | JP 1999-131583 | 19990512 |
| JP 3234980 | B2 | 20011204 | | |

PRIORITY APPLN. INFO.: US 1990-522996 A 19900514
JP 1991-199757 A3 19910510

OTHER SOURCE(S): MARPAT 116:214841
GI



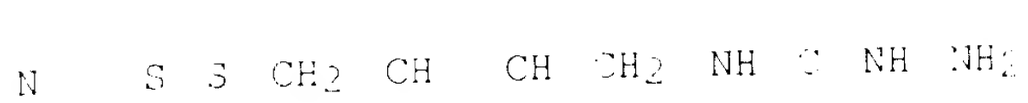
I

AB Anthracycline derivs. I [R1 = NHCONH(CH2)nSSR8, NHCONHNHCONH(CH2)nSSR8, NHCSNH(CH2)mCH:CH(CH2)nSSR8, NHCO2(CH2)nSSR8, NHArCONH(CH2)nSSR8, etc.; m, n = 1-10; R8 = (substituted) 2-pyridyl, -phenyl; Ar = phenylene; R2 = Me, CH2OH, CH2OCO(CH2)3Me, CH2OCOCH(OEt)2; R3 = OMe, OH, H; R4 = NH2 NHCOCF3, 4-morpholinyl, 3-cyano-4-morpholinyl, 1-piperidinyl, NHCH2Ph, N(CH2Ph)2, etc.; R5 = OH, tetrahydropyranyloxy, H; R6 = OH, H; R6 .noteq. OH when R5 = OH or tetrahydropyranyloxy], related compds., and their **conjugates** with ligands and antibodies, were prepd. Thus, 1-amino-4-[(2-pyridinyl)dithio]-2-butene-HCl (prepn. given) was treated with di(2-pyridyl) thionocarbonate and the product formed was condensed with Me3CO2CNHNH2. Deprotection of the resulting product by CF3CO2H gave N-[4-(2-pyridinyl)dithio]-2-butenyl]hydrazinecarbothioamide. This was condensed with adriamycin-HCl to give adriamycin 13-N-4-[(2-pyridinyl)dithio]-2-butenylhydrazinecarbothioamide thiosemicarbazene.cntdot.HCl (II). The **immunoconjugate** of II with thiolated monoclonal antibody 5E9 had IC50 of 3.0 .times. 10l-7M against Burkitt's lymphoma cells.

IT **133701-16-3P 140691-64-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for anticancer **immunoconjugates**)

RN 133701-16-3 HCAPLUS
CN Hydrazinecarboxamide, N-[2-(2-pyridinyldithio)ethyl]- (9CI) (CA INDEX NAME)

RN 140691-64-1 HCAPLUS
CN Hydrazinecarbothioamide, N-[4-(2-pyridinyldithio)-2-butenyl]- (9CI) (CA INDEX NAME)

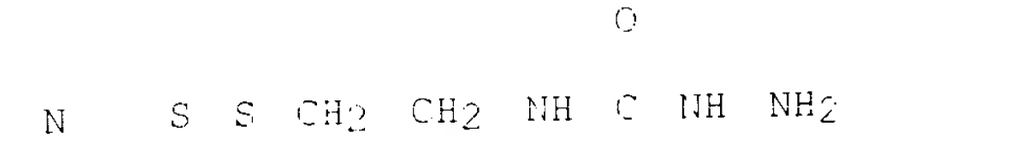


L9 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:253907 HCAPLUS
DOCUMENT NUMBER: 114:253907
TITLE: New hydrazone derivatives of Adriamycin and their **immunoconjugates** - a correlation between acid stability and cytotoxicity
AUTHOR(S): Kaneko, Takushi; Willner, David; Monkovic, Ivo; Knipe, Jay O.; Braslawsky, Gary R.; Greenfield, Robert S.; Vyas, Dolatrai M.
CORPORATE SOURCE: Bristol-Myers Squibb Co., Wallingford, CT, 06492-7660, USA
SOURCE: Bioconjugate Chemistry (1991), 2(3), 133-41
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New N-substituted hydrazine linkers were synthesized and their hydrazone derivs. of adriamycin were prepd. The adriamycin derivs. were **conjugated** with a monoclonal antibody, 5E9. The release rate of adriamycin from the hydrazones and from some of the **conjugates** was studied, and their relationship to the cytotoxicity against 5E9-pos. Daudi cells was investigated.

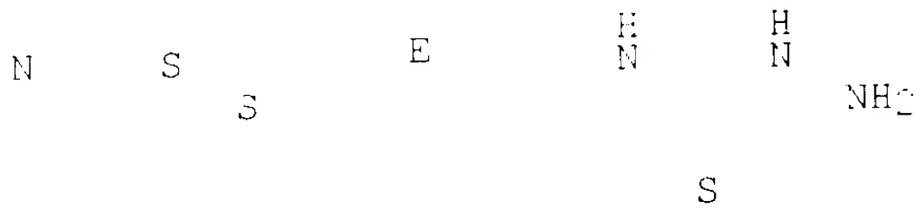
IT **133701-16-3P 133701-22-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with adriamycin, hydrazone from)

RN 133701-16-3 HCAPLUS
CN Hydrazinecarboxamide, N-[2-(2-pyridinyldithio)ethyl]- (9CI) (CA INDEX NAME)

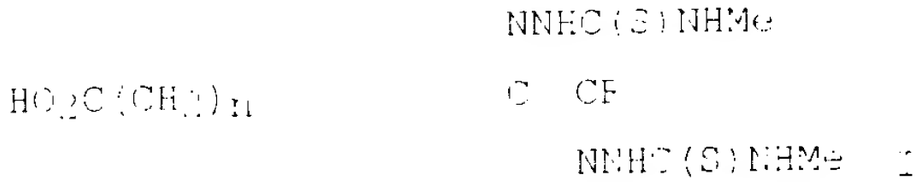


RN 133701-22-1 HCAPLUS
CN Hydrazinecarbothioamide, N-[4-(2-pyridinyldithio)-2-butenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



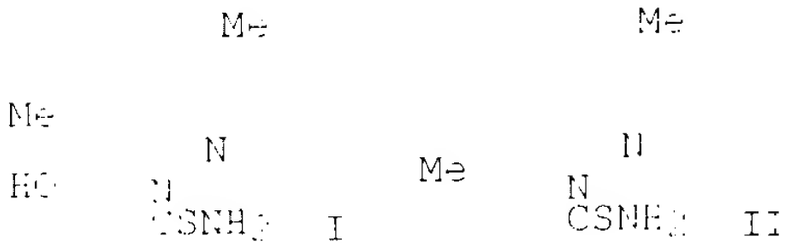
L9 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:201883 HCAPLUS
DOCUMENT NUMBER: 114:201883
TITLE: Radiolabeling of protein with radioisotopes of copper using p-carboxyalkylphenylglyoxal bis-(4N-methylthiosemicarbazone) (TSC) **bifunctional** chelates
AUTHOR(S): McPherson, D. W.; Umbricht, G.; Knapp, F. F., Jr.
CORPORATE SOURCE: Health Saf. Res. Div., Oak Ridge Natl., Oak Ridge, TN, 37831-6012, USA
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1990), 28(8), 877-99
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:201883
GI



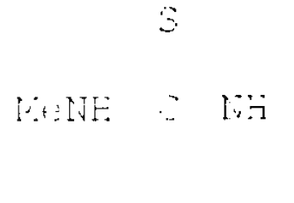
AB A series of p-carboxyalkylphenylglyoxal and p-carboxyalkyl-1,2-diketobis(N4-methylthiosemicarbazone) **bifunctional** ligands I (R = H or Me, n = 1-9) were prepd. and evaluated for use in binding radioisotopes of Cu to antibodies. An improved synthesis of the requisite .alpha.-keto aldehyde and 1,2-diketone substrates used for derivatization to the bis-TSC **bifunctional** chelates was developed. This approach utilizes a modified Kornblum method and provides a simple alternative to the usual method for fabrication of the 1,2-bis ligands, which avoids the use of highly toxic SeO2 for oxidn. of substituted acetophenones to 1,2 dicarbonyl compds. The overall yields of the bis-TSC chelates using this procedure were 8-60%. The effects of the alkyl chain length and substitution on the C-2 position on **bifunctional** chelates for attaching radioisotopes of copper to proteins were studied. Following complexing 64Cu or 67Cu to the bis chelate, the acid moiety of the chelate was activated as the tetrafluorophenyl ester. The copper-labeled activated chelate was attached to bovine serum albumin under mild conditions in 3% to 40% yield. The shorter chain analog of the chelates from the 1,2-diketones give the highest radiolabeling yields.
IT **6610-29-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carboxyalkylphenylglyoxal derivs.)
RN 6610-29-3 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)

L9 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:150963 HCAPLUS

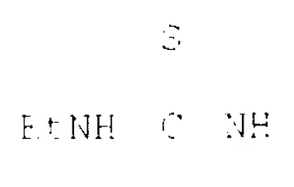
DOCUMENT NUMBER: 108:150362
TITLE: Reactions of 1,4-**bifunctional** derivatives of hydrazine with 1,3-diketones
AUTHOR(S): Selenin, F. N.; Slod, O. V.; Tomchin, A. B.
CORPORATE SOURCE: Voen.-Med. Akad., Leningrad, USSR
SOURCE: Zhurnal Obshchei Khimii (1987), 57(3), 584-95
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 108:150362
GI



AB Hydrazine derivs., e.g., aminoguanidine nitrate, PhNHCONHNH2, amidrazonium iodides, R1HNCSNHNH2 (R1 = H, Me, Et) condense with RCOCH2COR (R = Me, Ph) to give, depending on reaction conditions, 5-hydroxy- and 5-hydrazino-2-pyrazolines, mono- and bis(hydrazones), and also the corresponding pyrazoles. Thus, treating MeCOCH2COMe with H2NCSNHNH2 gave pyrazoline I which dehydrated in refluxing solvent to give the corresponding pyrazole II. Addnl. obtained was R1NHN:CRCH2CR:NNHR1 [R = Me, R1 = CONHPh, C(:NH)(NH2).HNO3].
IT **6610-29-3**, 4-Methyl-3-thiosemicarbazide **13431-34-0**, 4-Ethyl-3-thiosemicarbazide
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation and cyclocondensation of, with diketones)
RN 6610-29-3 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)



RN 13431-34-0 HCAPLUS
CN Hydrazinecarbothioamide, N-ethyl- (9CI) (CA INDEX NAME)



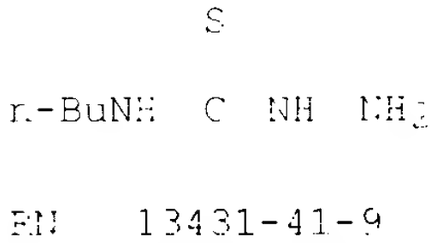
L9 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:196867 HCAPLUS
DOCUMENT NUMBER: 106:196867
TITLE: Polymers containing the [2H]-1,2,4-triazoline-3-thione ring
AUTHOR(S): Katritzky, Alan R.; Cato, Stephen J.; Heilmann, Steven M.; Rasmussen, Jerald K.; Krepski, Larry R.

CORPORATE SOURCE: Chem. Dep., Univ. Florida, Gainesville, FL, 32611, USA
SOURCE: Journal of Polymer Science, Part A: Polymer Chemistry (1987), 25(1), 311-26
CODEN: JPACEC; ISSN: 0887-624X
DOCUMENT TYPE: Journal
LANGUAGE: English

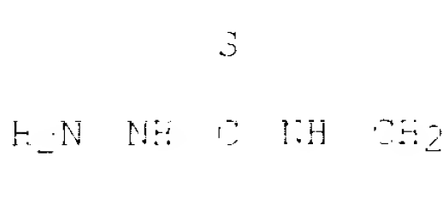
AB High-mol.-wt. polymers contg. [2H]-1,2,4-triazoline-3-thione rings are prepd. by the condensations of diisothiocyanates with bis(acid hydrazides) to give intermediate polymeric acylthiosemicarbazides that are ring-closed by refluxing in 1M aq. sodium carbonate. Thermal cyclization of the polymeric acylthiosemicarbazides leads to **crosslinked** insol. products. The acylation of bis(thiosemicarbazides) with bis(acid chlorides) produces polymers of a similar structure but lower mol. wt.

IT **6610-31-7P**, 4-Butylthiosemicarbazide **13431-41-9P**, 4-Benzylthiosemicarbazide
PL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction with Et imido ester hydrochlorides)

RN 6610-31-7 HCAPLUS
CN Hydrazinecarbothioamide, N-butyl- (9CI) (CA INDEX NAME)



RN 13431-41-9 HCAPLUS
CN Hydrazinecarbothioamide, N-(phenylmethyl)- (9CI) (CA INDEX NAME)

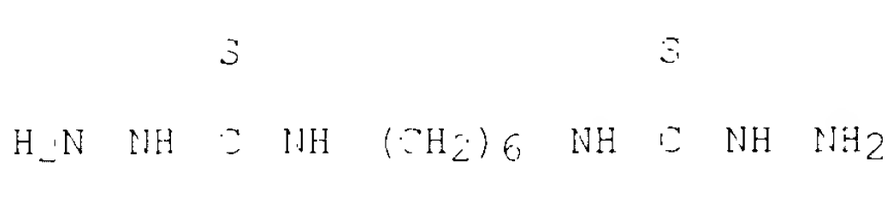


IT **108144-98-5P**
PL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 108144-98-5 HCAPLUS
CN 1,4-Benzenedicarbonyl dichloride, polymer with N,N'-1,6-hexanediylbis[hydrazinecarbothioamide] (9CI) (CA INDEX NAME)

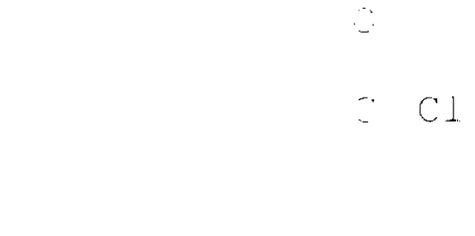
CM 1

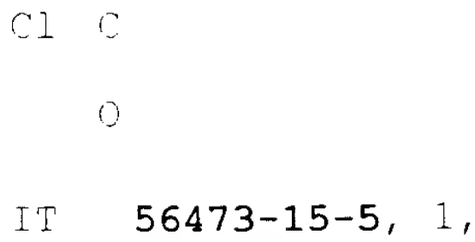
CRN 56473-15-5
CMF C8 H20 N6 S2



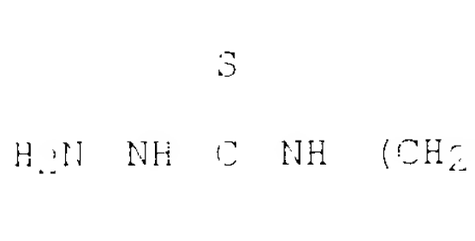
CM 2

CRN 100-20-9
CMF C8 H4 Cl2 O2

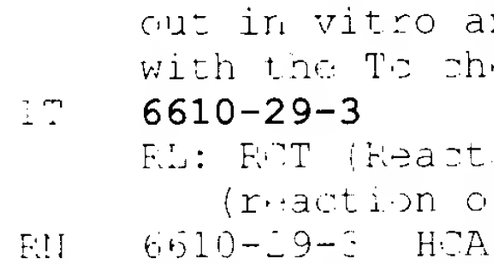




IT **56473-15-5**, 1,6-Hexanebis(thiosemicarbazide)
BL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Et benzimidoate hydrochloride)
RN 56473-15-5 HCAPLUS
CN Hydrazinecarbothioamide, N,N'-1,6-hexanediylbis- (9CI) (CA INDEX NAME)

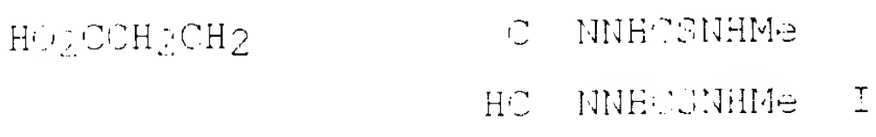


L9 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:520711 HCAPLUS
DOCUMENT NUMBER: 105:120711
TITLE: Search for technetium-99m labeled DTS **bifunctional** radiopharmaceutical: role of functional groups in myocardial accumulation
AUTHOR(S): Hosotani, Takeo; Yokoyama, Akira; Arano, Yasushi; Horiuchi, Kazuko; Saji, Hideo; Torizuka, Kanji
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Applied Radiation and Isotopes (1986), 37(6), 505-11
CODEN: ARISEF; ISSN: 0883-2889
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:120711
AB Various mols. contg. a neutral 99mTc-dithiosemicarbazone (DTS) structure as the Tc chelating site, along with various functional groups (NH2, CO2H or iso-Bu group with diverse charge) were tested for their chem. or biol. functions. The study on the effect of those functional groups was carried out in vitro and in vivo. The validity of introducing an NH2 group along with the Tc chelating site DTS for myocardial accumulation is discussed.
IT **6610-29-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phenylglyoxals)
RN 6610-29-3 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)

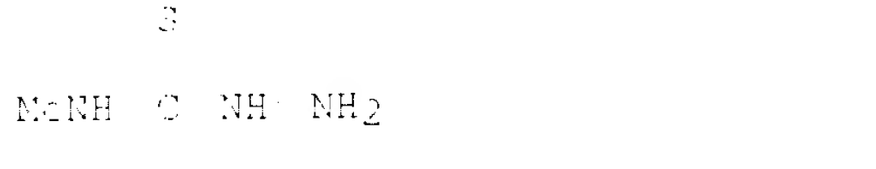


L9 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:438343 HCAPLUS

DOCUMENT NUMBER: 105:68342
TITLE: Synthesis and evaluation of a new **bifunctional** chelating agent for technetium-99m labeling proteins: p-carboxyethylphenylglyoxal-di(N-methylthiosemicarbazone)
AUTHOR(S): Arano, Yasushi; Yokoyama, Akira; Magata, Yasuhiro; Saji, Hideo; Horiuchi, Kazuko; Torizuka, Kanji
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606, Japan
SOURCE: International Journal of Nuclear Medicine and Biology (1986), 13(6), 425-30
CODEN: IJNMCI; ISSN: 0047-0740
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB A new **bifunctional** chelating agent, p-carboxyethylphenylglyoxal-di(N-methylthiosemicarbazone) (I), contg. a di(N-methylthiosemicarbazone) as the Tc coordinating site and an aralkyl carboxylate site for the protein **conjugation** was synthesized. Coupling to human serum albumin (HSA), selected as a model protein, was carried out by the phosphorylazide method using diphenylphosphoryl azide (DPPA). The **conjugation** level of I to HSA played a crit. role in its biol. evaluation. A 99mTc-I-HSA with high in vivo stability was obtained when I was coupled to HSA at 1:1 molar ratio. This compd. showed similar in vivo stability to 131I-labeled HSA in mice and rabbits.
IT **6610-29-3**
RL: PRP (Properties)
(**conjugation** of, with acetylphenylpropionic acid)
RN 6610-29-3 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)



L9 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:184835 HCAPLUS
DOCUMENT NUMBER: 102:184835
TITLE: p-Glyoxalphenylalkylcarboxylic acid bis(thiosemicarbazone) derivatives
PATENT ASSIGNEE(S): Nihon Medi-Physics Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| JP 59193870 | A2 | 19841102 | JP 1983-68850 | 19830419 |
| JP 04016465 | B1 | 19920324 | | |
| AU 8319934 | A1 | 19841025 | AU 1983-19934 | 19831006 |
| AU 561568 | B2 | 19870514 | | |
| US 4550111 | A | 19851217 | US 1983-538684 | 19831007 |
| CA 1206476 | A1 | 19860701 | CA 1983-438615 | 19831007 |

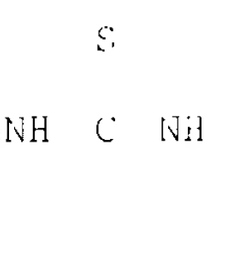
PRIORITY APPLN. INFO.: JP 1983-68850 19830419
JP 1983-68851 19830419

OTHER SOURCE(S): CASREACT 102:184833

AB **Bifunctional** ligand title derivs. 4-HO2C(CH2)nC6H4C(:NNHCSNHMe)CH:NNHCSNHMe I (n = 1-4) were prepd. by reaction of 4-HO2C(CH2)nC6H4COCHO (II) with H2NNHCSNHMe (III). I are useful as radioactive diagnostic reagents labeled with radioactive metals. Thus, refluxing 1.76 g 4-HO2CCH2C6H4COMe with 1.22 g SeO2 in dioxane 7 h gave II (n = 1), which (in EtOH) was added to 2.1 g III in 15 mL N aq. HCl at 60.degree. to ppt. 1.1 g I (n = 1).

IT **6610-29-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phenylglyoxal derivs.)

RN 6610-29-3 HCAPLUS
CN Hydrazinecarbothioamide, N-methyl- 9CI) (CA INDEX NAME)




L9 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:25570 HCAPLUS
DOCUMENT NUMBER: 102:25570
TITLE: Basic polymers
PATENT ASSIGNEE(S): Asahi Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 59152905 | A2 | 19840831 | JP 1983-26892 | 19830222 |
| JP 04069169 | B4 | 19921105 | | |

PRIORITY APPLN. INFO.: JP 1983-26892 19830222
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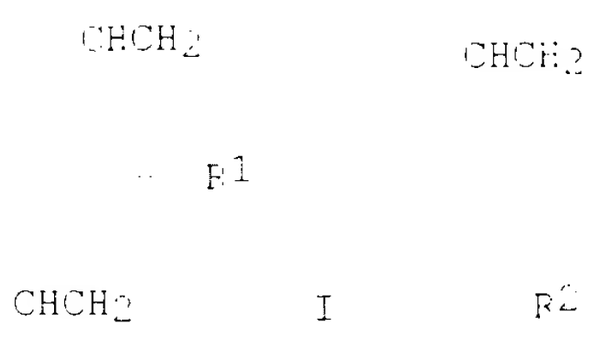
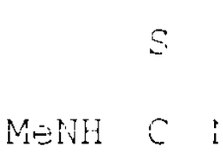


AB The 2-50:50-98 (molar) I-II copolymers substituted with 10-99 mol% (based on total benzene rings) nuclear -COX group (X = OH, Cl) were treated with (methyl)thiosemicarbazide, an alkali, and then a nitrite salt in HNO3 to obtain the **crosslinked** title polymers having 10-98 mol% (based on total benzene rings) III groups (on benzene rings), useful for anion exchangers (R's = H, C1-4 hydrocarbyl). Thus, 12:88 m-divinylbenzene-styrene copolymer was subjected to a Friedel-Crafts reaction with oxalyl chloride in CS2 to obtain a chlorocarbonyl deriv. (I, 58 mol% COCl), which (11.5-4 g) was mixed with 150 mL EtOH and 21.0 g methylthiosemicarbazide, stirred under reflux for 2 h, filtered, washed with acetone-H2O, heated with 60 g NaOH in 300 mL water at 100.degree. for 1.5 h, filtered, washed with water, suspended in 100 mL water, and treated with 6.2 g NaNO2 and 50 mL conc. HNO3 at 45.degree. for 2 h to give 13.345 g polymer (52 mol % 4-methyltriazole group) having exchange capacity (HCl form) 1.71 mequiv/g.

IT **6610-29-3**
RL: USES (Uses)
(in triazole group-contg. styrene deriv. polymer anion exchanger manuf.)

RN 6610-29-3 HCAPLUS

CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)



MeNH C NH $NH_2$

L9 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1981:463041 HCAPLUS
DOCUMENT NUMBER: 95:63081
TITLE: 1-Oxopropanaldehydebis(thiosemicarbazone) derivatives
INVENTOR(S): Yakoyama, Akira; Anano, Yasushi
PATENT ASSIGNEE(S): Nihon Medi-Physics Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 24464 | A1 | 19810311 | EP 1980-100199 | 19800110 |
| EP 24464 | B1 | 19830615 | | |
| R: BE, DE, FR, GB, NL, SE | | | | |
| JP 56034564 | A2 | 19810406 | JP 1979-110831 | 19790829 |
| JP 56034565 | A2 | 19810406 | JP 1979-110832 | 19790829 |
| AU 8054721 | A1 | 19810305 | AU 1980-54721 | 19800118 |
| AU 627412 | B2 | 19820805 | | |
| US 4278602 | A | 19810701 | US 1980-113341 | 19800118 |
| CA 1175418 | A1 | 19841002 | CA 1980-343997 | 19800118 |
| US 4538248 | A | 19850806 | US 1980-177947 | 19800814 |

PRIORITY APPLN. INFO.: JP 1979-110831 19790829
JP 1979-110832 19790829
US 1980-113341 19800118

AB A radiolabeled diagnostic agent prepd. from a protein and a radioactive element and a **bifunctional** chelating agent is quite stable. The

chelating agent 3-carboxy-2-oxopropionaldehyde bis(N-methylthiosemicarbazone) (I) [78277-30-2], prepd. from Et diethoxyacetate [10495-09-7] and N-methylthiosemicarbazide [**6610-29-3**] and hydrolysis of the resulting 3-ethoxycarbonyl-2-oxopropionaldehyde bis(N-methylthiosemicarbazone) [78277-63-5], was converted to a mixed anhydride by treatment with iso-Bu chloroformate. Human serum albumin was mixed with the anhydride and subjected to dialysis followed by lyophilization. The albumin-I complex was treated with 99mTc (10.5mCi) at pH 5.6 in the form of a pertechnetate and reduced with SnCl2 soln. to yield a 99mTc-albumin-I complex useful as a radioactive diagnostic agent. The complex had a labeling efficiency of .apprx.100%, showed higher blood levels for longer times than conventional 99mTc-albumin complexes, and was quite stable.

IT **6610-29-3**
RL: RCT (Reactant); FACT (Reactant or reagent)
(reaction of, with Et diethoxyacetoacetate)

RN 6610-29-3 HCAPLUS

CN Hydrazinecarbothioamide, N-methyl- (9CI) (CA INDEX NAME)

S

MeNH C NH NH2

L9 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1979:612698 HCAPLUS
DOCUMENT NUMBER: 91:212698
TITLE: Aqueous dispersions of copolymers with carbonyl groups and containing hydrazine derivatives
INVENTOR(S): Ley, Gregor; Penzel, Erich; Rebafka, Walter; Bott, Kaspar
PATENT ASSIGNEE(S): BASF A.-G., Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 3516 | A1 | 19790822 | EP 1979-100168 | 19790119 |
| EP 3516 | B1 | 19810401 | | |
| R: BE, CH, DE, FR, GB, IT, NL, SE | | | | |
| DE 2803070 | A | 19810910 | DE 1979-2803 | 19790116 |
| CA 1161786 | A1 | 19830809 | CA 1979-320224 | 19790124 |
| DK 7900917 | A | 19790727 | DK 1979-917 | 19790125 |
| DK 151999 | B | 19880111 | | |
| DK 151999 | C | 19880613 | | |
| NO 790155 | A | 19790727 | NO 1979-255 | 19790125 |
| NO 156694 | B | 19870202 | | |
| NO 156694 | C | 19870513 | | |
| ES 477135 | A1 | 19791101 | ES 1979-477135 | 19790125 |
| AT 7900557 | A | 19801015 | AT 1979-557 | 19790125 |
| AT 365566 | B | 19810526 | | |
| JP 54110048 | A2 | 19790829 | JP 1979-7291 | 19790126 |
| JP 61006861 | B4 | 19860301 | | |

PRIORITY APPLN. INFO.: DE 1978-2803258 19780126

AB Aq. coating dispersions of reaction products of polycarboxylic acid hydrazides, bis(semicarbazides), or CO(NHNH2)2 with aldehyde or ketone carbonyl group-contg. vinyl polymers are stabilized against hydrolysis during storage by addn. of 0.0001-0.02 mol Cu, Fe, Mn, V, Sn, Cr, and(or) Ni per mol hydrazine deriv.; the metal salts are also **crosslinking** catalysts. Thus, 200 parts 17.5% aq. 25:50:25 succinic dihydrazide-glutaric dihydrazide-adipic dihydrazide dispersion and 0.06 part CuSO4 were added to a copolymer dispersion, prepd. from Me acrylate 375, Bu acrylate 90, acrylic acid 10, and acrolein 25 parts, to give a storage-stable dispersion. A room temp.-dried coating film swelled in DMF picking up 110-210% of its wt. in 1 day, but did not dissolve.

IT **51440-70-1D**, reaction products with carbonyl group-contg. polymers
PL: TEM (Technical or engineered material use); USES (Uses)
(coatings, stabilization of, with transition metal salts)

RN 51440-70-1 HCAPLUS

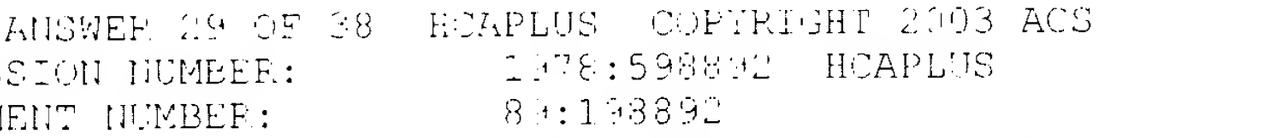
CN Hydrazinecarboxamide, N,N'-1,6-hexanediylbis- (9CI) (CA INDEX NAME)

L9 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:598892 HCAPLUS
DOCUMENT NUMBER: 89:198892
TITLE: Self-**crosslinkable** polyurethanes
INVENTOR(S): Winkelmann, Hans Dieter; Wolf, Karl Heinz; Oertel, Harald; Weimann, Norbert
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 53 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2707659 | A1 | 19780824 | DE 1977-2707659 | 19770223 |
| US 4153775 | A | 19790508 | US 1978-879504 | 19780221 |
| JP 53105599 | A2 | 19780913 | JP 1978-18646 | 19780222 |
| GB 1597989 | A | 19810916 | GB 1978-7034 | 19780222 |
| NL 7802056 | A | 19780825 | NL 1978-2036 | 19780223 |

PRIORITY APPLN. INFO.: DE 1977-2707659 19770223

GI



AB Urethane I [68125-44-0] and similar diols contg. caprolactam (II) [105-60-2]-blocked isocyanate groups were prepd. for use in the manuf. of self-**crosslinking** polyurethane elastomers. Thus, an adduct of 2

mol II and 1 mol bis(4-isocyanatophenyl)methane (III) [101-68-8] was treated with H.NN(CH2CHMeOH)2 [62723-38-0] to prep. I. Adipic acid-1,6-hexanediol-neopentyl glycol copolymer (mol. wt. 1875) 500, MeN(CH2CHMeOH)2 10.58, I 37.2, and III 163.3 parts were used to prep. a prepolymer which was treated with ethylenediamine and diisocyanatohexane to prep. a **crosslinkable** copolymer [68125-45-1]. A film prepd. from the copolymer and heated at 130.degree. for 30 min was insol. in DMF at 50.degree..

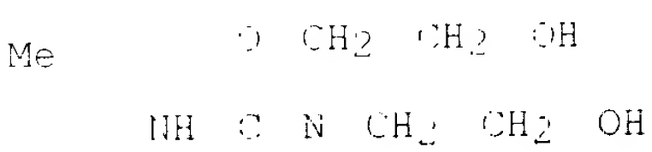
IT **68125-51-9**
PL: USES (Uses)
(rubber, **crosslinked**)

RN 68125-51-9 HCAPLUS

CN .beta.-Alanine, N-(hydrazinocarbonyl)-, hydrazide, polymer with N-[3-[[[bis(2-hydroxyethyl)amino]carbonyl]amino]-4-methylphenyl]hexahydro-2-oxo-1H-azepine-1-carboxamide, 2,2-dimethyl-1,3-propanediol, hexanedioic acid, 1,6-hexanediol, 1,1'-methylenebis[4-isocyanatobenzene] and 1,1'-(methylimino)bis[2-propanol] (9CI) (CA INDEX NAME)

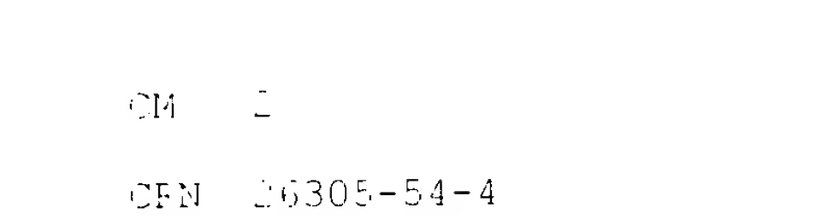
CM 1

CRN 68125-43-4
CMF C19 H28 N4 O5



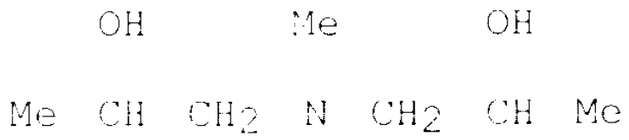
CM 2

CRN 26305-54-4
CMF C4 H11 N5 O2



CM 3

CRN 4402-30-6
CMF C7 H17 N O2



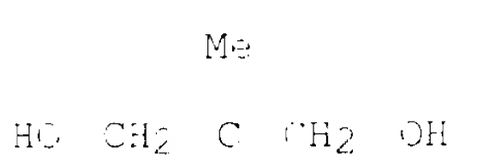
CM 4

CRN 6[illegible]9-11-3
CMF C[illegible] H14 O2



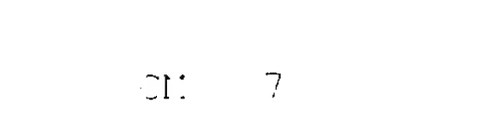
CM 5

CRN 1[illegible]6-30-7
CMF C[illegible] H12 O2



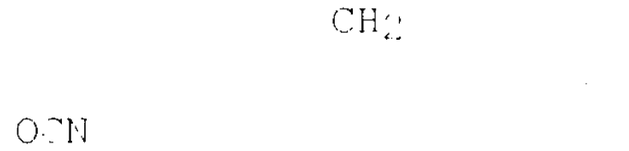
CM 6

CRN 1[illegible]4-04-9
CMF C[illegible] H1[illegible] O4



CM 7

CRN 1[illegible]1-63-8
CMF C15 H10 N2 O2

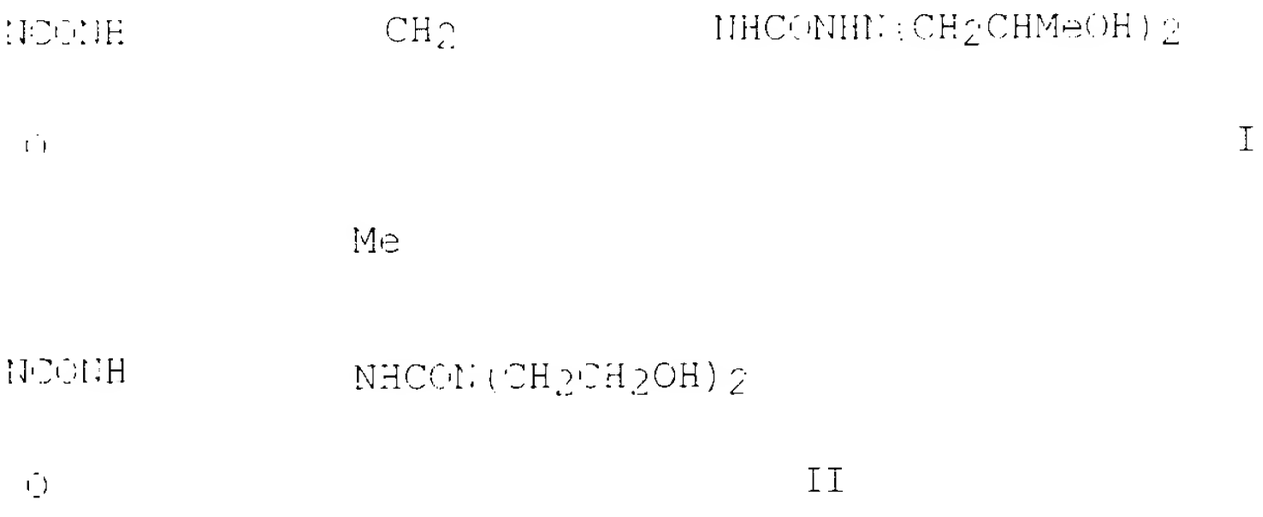


L9 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:598891 HCAPLUS
DOCUMENT NUMBER: 89:198891
TITLE: Isocyanate adduct diols
INVENTOR(S): Winkelmann, Hans Dieter; Wolf, Karl Heinz; Oertel, Harald; Weimann, Norbert
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 50 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2707660 | A1 | 19780824 | DE 1977-2707660 | 19770223 |
| DE 2707660 | C2 | 19851219 | | |
| US 4211699 | A | 19800708 | US 1978-879740 | 19780221 |
| JP 53109428 | A2 | 19780913 | JP 1978-18647 | 19780222 |
| JP 60053017 | B4 | 19851122 | | |

PRIORITY APPLN. INFO.: DE 1977-2707660 19770223
GI



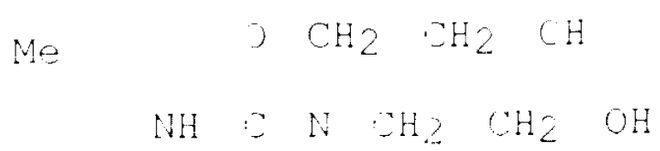
AB I [68125-44-0], II [68125-48-4], and 3 similar diols were prepd. and used for the manuf. of self-**crosslinking** polyurethane elastomers. Thus, an adduct of 2 mol caprolactam [105-60-2] and 1 mol bis(4-isocyanatophenyl)methane (III) [101-68-8] was treated with H2NN(CH2CHMeOH)2 [68723-38-0] to prep. I. I 37.2, adipic acid-neopentyl glycol-1,6-hexanediol copolymer (mol. wt. 1875) 500, MeN(CH2CHMeOH)2 10.68, and III 163.3 parts were used to prep. a prepolymer which was treated with ethylenediamine and OCN(CH2)6NCO to prep. a polyurethane [68125-45-1]. A film prepd. from the polyurethane and heated at 150.degree. for 30 min was insol. in DMF at 80.degree..

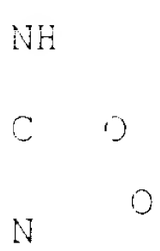
IT **68125-51-9**
PL: USES (Uses)
(rubber, **crosslinked**)

RN 68125-51-9 HCAPLUS
CN .beta.-Alanine, N-(hydrazinocarbonyl)-, hydrazide, polymer with N-[3-[[[bis(2-hydroxyethyl)amino]carbonyl]amino]-4-methylphenyl]hexahydro-2-oxo-1H-azepine-1-carboxamide, 2,2-dimethyl-1,3-propanediol, hexanedioic acid, 1,6-hexanediol, 1,1'-methylenebis[4-isocyanatobenzene] and 1,1'-(methylimino)bis[2-propanol] (9CI) (CA INDEX NAME)

CM 1

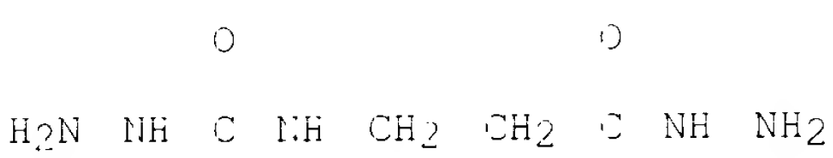
CRN 68125-48-4
CMF C19 H28 N4 O5





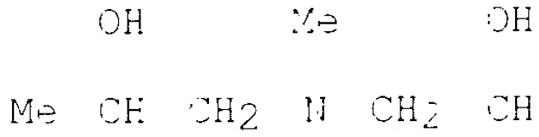
CM 2

CRN 20305-54-4
CMF C4 H11 N5 O2



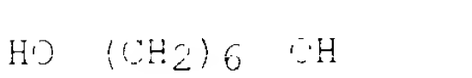
CM 3

CRN 4402-30-6
CMF C7 H17 N O2



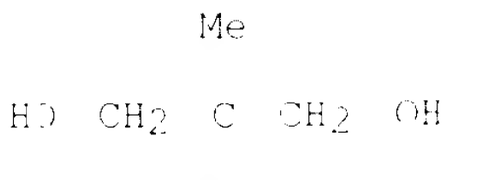
CM 4

CRN 619-11-8
CMF C6 H14 O2



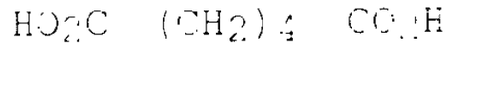
CM 5

CRN 126-30-7
CMF C5 H12 O2



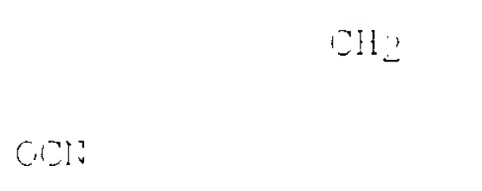
CM 6

CRN 124-04-9
CMF C6 H10 O4

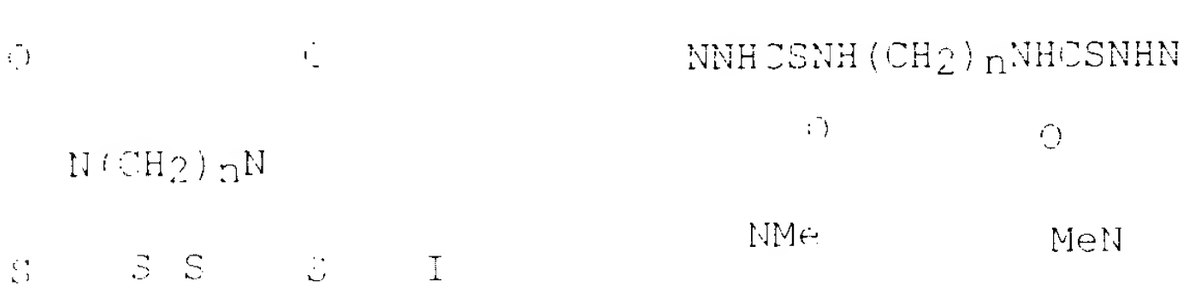


CM 7

CRN 101-66-8
CMF C15 H10 N2 O2



L9 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1976:59241 HCAPLUS
DOCUMENT NUMBER: 85:192481
TITLE: Bis(thiosemicarbazido)alkanes and their main optical characteristics
AUTHOR(S): Zimenkovskii, B. S.; Turkevich, N. M.
CORPORATE SOURCE: Lvov Med. Inst., Lvov, USSR
SOURCE: Farmatsevtichnii Zhurnal (Kiev) (1976), (4), 22-6
CODEN: FRZKAP; ISSN: 0367-3057
DOCUMENT TYPE: Journal
LANGUAGE: Ukrainian
GI

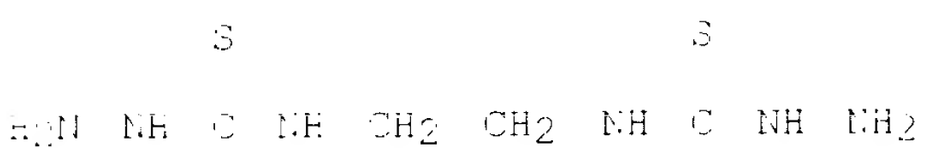


AB Hydrazinolysis of .alpha.,.omega.-bis(thiazino)alkane derivs. I (n = 2,6) afforded H2NNHCSNH(CH2)nNHCSNHNH2 (II), which reacted with 1-methylisatin to give bisthiosemicarbazones III. II had a single uv absorption max. at

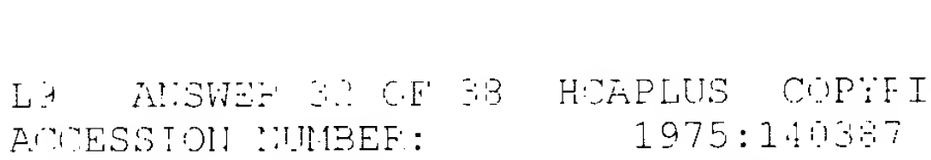
238-42 nm, corresponding to p-.pi. **conjugation**; III had uv max. at 238-46, 273-4, and 349-54 nm, corresponding to p-.pi., p-.pi.*, and the hydrazone chromophore, resp.

IT **1728-65-0P 56473-15-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and uv of, and reaction with methylisatin)

RN 1728-65-0 HCAPLUS
CN Hydrazinecarbothioamide, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)



RN 56473-15-5 HCAPLUS
CN Hydrazinecarbothioamide, N,N'-1,6-hexanediylbis- (9CI) (CA INDEX NAME)



L9 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1975:140387 HCAPLUS
DOCUMENT NUMBER: 82:140387
TITLE: Steroid haptens
INVENTOR(S): Torelli, Vesperto; Pierdet, Andre
PATENT ASSIGNEE(S): Roussel-UCLAF
SOURCE: Ger. Offen., 45 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2429040 | A1 | 19750109 | DE 1974-2429040 | 19740618 |
| DE 2429040 | C2 | 19851031 | | |
| FR 2235949 | A1 | 19750131 | FR 1973-22114 | 19730618 |
| SE 7407106 | A | 19741219 | SE 1974-7108 | 19740529 |
| SE 402461 | C | 19781012 | | |
| BE 816157 | A1 | 19741217 | BE 1974-145535 | 19740617 |
| NL 7407941 | A | 19741220 | NL 1974-8041 | 19740617 |
| DK 7403222 | A | 19750210 | DK 1974-3222 | 19740617 |
| US 3922291 | A | 19751125 | US 1974-479889 | 19740617 |
| CA 1029841 | A | 19760411 | CA 1974-3041 | 19740617 |
| ES 427318 | A1 | 19760916 | ES 1974-427318 | 19740617 |
| BE 816457 | A0 | 19750121 | BE 1974-4979 | 19740618 |
| JP 50016451 | A2 | 19750205 | JP 1974-69309 | 19740618 |
| JP 54[illegible] | B4 | 19831004 | | |
| AU 7470[illegible] | A1 | 19751218 | AU 1974-70148 | 19740618 |
| GB 1[illegible] | A | 19770601 | GB 1974-27121 | 19740618 |
| GB 1[illegible] | A | 19770629 | GB 1977-3645 | 19740618 |
| AT 7405[illegible] | A | 19770915 | AT 1974-5043 | 19740618 |
| ES 448013 | A1 | 19770701 | ES 1976-448013 | 19760517 |
| ES 448012 | A1 | 19770701 | ES 1976-448012 | 19760517 |

| | | | | |
|---|---|---|---|---|
| AT 351690 | B | 19790810 | AT 1976-9863 | 19761210 |
| AT [illegible] | A | 19790115 | | |
| JP [illegible] | A2 | 19830530 | JP 1982-184370 | 19821019 |
| JP [illegible] | B4 | 19840401 | | |
| JP [illegible] | A | 19830530 | JP 1982-184371 | 19821019 |
| JP [illegible] | B4 | 19850116 | | |
| JP [illegible] | A | 19791122 | JP 1964-73124 | 19641213 |
| JP [illegible] | B4 | 19870714 | | |

PRIORITY APPLN. INFO.: FR 1972-22114 19720613
AT 1974-9043 19741122

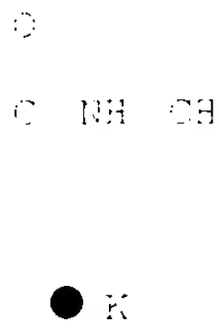
GI For diagram(s), see printed CA Issue.

AB Estratrienols I [R = H, R1 = (CH2)3CO2H, (CH2)10CO2H; RR1 = NOCH2CO2H, NHCOCH2CO2H, NOCH2CO2H; R2 = H, (CH2)3CO2H; R3 = H, HO; R4 = H; R5 = HO, R4R5 = O] (10 compds.) were prepd. I [R = R1 = R3 = R4 = H; R2 = (CH2)3CO2H, R5 = HO] (II) and I [R = R1 = R3 = H, R2 = (CH2)3CO2H, R4R5 = O] formed **conjugates** with bovine serum albumins. Thus, secoestrenol III was successively epoxidized, sapond., treated with CH2:CHCH2MgBr, hydrolyzed, cyclized, aromatized, sapond., benzylated, oxidized, treated with (EtO)2POCH2CO2Me, and hydrogenated to give I [R = R1 = R3 = R4 = H, R2 = (CH2)3CO2H, R5 = HO]. 6-Dehydro-19-nortestosterone acetate was successively treated with the tetrahydropyranyl ether of ClMg(CH2)4OH, sapond., oxidized, and dehydrogenated to give I [R = H, R1 = (CH2)3CO2H, R2 = R3 = H, R4R5 = O].

IT **3242-64-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxyestratrienone)

RN 3242-64-6 HCAPLUS

CN Glycine, N-(hydrazinocarbonyl)-, monopotassium salt (9CI) (CA INDEX NAME)



● K

L9 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:404780 HCAPLUS
DOCUMENT NUMBER: 81:4780
TITLE: Polyurethane coatings
INVENTOR(S): Zorn, Bruno; Noll, Klaus; Oertel, Harald; Traeubel, Hanno
PATENT ASSIGNEE(S): Bayer A.-G.
SOURCE: Ger. Offen., 35 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2211756 | A1 | 19731113 | DE 1972-2211756 | 19720504 |
| DE 2211756 | B2 | 19791018 | | |
| DE 2211756 | C3 | 19800626 | | |
| CA 1003712 | A1 | 19770118 | CA 1973-169961 | 19730425 |

| | | | | |
|---|---|---|---|---|
| JP 49032150 | A2 | 19740903 | JP 1973-47619 | 19730501 |
| JP 58002373 | B4 | 19830119 | | |
| IT [illegible] | A | 19750410 | IT 1973-49740 | 19731102 |
| BE [illegible] | A1 | 19731101 | BE 1973-130686 | 19731102 |
| NL [illegible] | A | 19731106 | NL 1973-6180 | 19731102 |
| NL [illegible] | B | 19850401 | | |
| NL [illegible] | C | 19850902 | | |
| ES [illegible] | A1 | 19760201 | ES 1973-414335 | 19731102 |
| FR [illegible] | A1 | 19731214 | FR 1973-16162 | 19730504 |
| GB [illegible] | A | 19760128 | GB 1973-21174 | 19730504 |

PRIORITY APPLN. INFO.: DE 1972-2221736 19720504

AB Solvent-stable polyurethanes, useful as light- and abrasion-resistant coatings for textiles, leather, and leather substitutes, are prepd. by mixing solns. of aliph. or cycloaliph. diisocyanate-contg. urethane prepolymers (essentially free of NCO or NH2 groups) in hydrocarbon-aliph. secondary alc. solvents with aliph. polyisocyanates, NCO functionality >2. Thus, heating adipic acid-1,4-butanediol copolymer (OH no. 31, mol. wt. 2100) 1890, OH-terminated dimethylsiloxane (OH no. 198, mol. wt. 600) 84, 1-isocyanato-3-(isocyanatomethyl)-3,5,5-trimethylcyclohexane 710, and xylene 4600 parts 2 hr at 80-100.deg. (NCO content 2.1%) and addn. of sufficient 374:4600 1-amino-3-(aminomethyl)-3,5,5-trimethylcyclohexane-MeOH soln. to give 25.deg. viscosity .sim. 150 P gives a soln. of clear, solid, EtOH-sol. adipic acid-1-amino-3-(aminomethyl)-3,5,5-trimethylcyclohexane-1,4-butanediol-1-isocyanato-3-(isocyanatomethyl)-3,5,5-trimethylcyclohexane copolymer [51200-60-4]. A 12 .mu. coating on textiles prepd. from this soln. with addn. of 30% (based on solids) com. hexamethylene diisocyanate [822-06-0]-based biuret-triisocyanate (I) cured 1 week at room temp. has very good alc. rub-fastness, compared with unsatisfactory-moderate in the presence of 0-20% I.

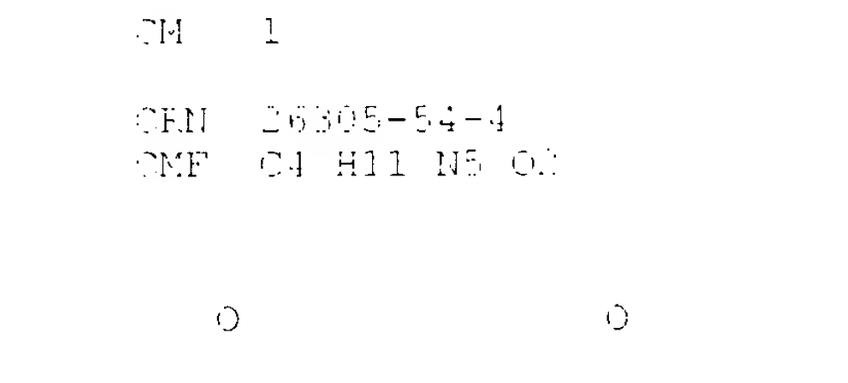
IT **52004-60-1**
PL: TEM (Technical or engineered material use); USES (Uses)
(coatings, for leather and textiles)

RN 52004-60-1 HCAPLUS

CN .beta.-Alanine, N-(hydrazinocarbonyl)-, hydrazide, polymer with hexanedioic acid, 1,6-hexanediol and 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethylcyclohexane (9CI) (CA INDEX NAME)

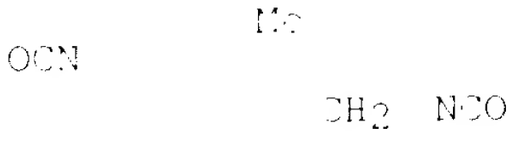
CM 1

CRN 26305-54-4
CMF C4 H11 N5 O2



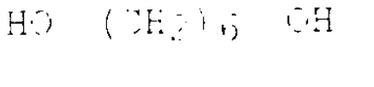
CM 2

CRN 4035-71-9
CMF C13 H18 N2 O2



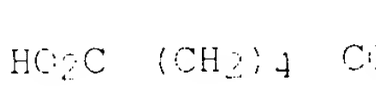
CM 3

CRN 119-11-8
CMF C6 H14 O2



CM 4

CRN 124-04-9
CMF C6 H10 O4



L9 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:27645 HCAPLUS
DOCUMENT NUMBER: 80:27645
TITLE: 4,4-Alkylenebissemicarbazides and their derivatives
INVENTOR(S): Sheppard, Chester S.; MacLeay, Ronald E.
PATENT ASSIGNEE(S): Pennwalt Corp.
SOURCE: U.S., 10 pp. Division of U.S. 3,585,200 (CA 75;77759k).
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3755238 | A | 19730828 | US 1970-59807 | 19700622 |
| US 3585200 | A | 19710615 | US 1966-556263 | 19660609 |

PRIORITY APPLN. INFO.: US 1966-556263 19660609

AB Substituted oxadiazolinones were treated with diamines to give alkylene bis(semicarbazides) which were used as monomers, blowing agents, and polymn. initiators. A mixt. contg. 50 g 2-phenyl-.DELTA.2-1,3,4-oxadiazolin-5-one [1199-02-6], 9.0 g ethylenediamine [107-15-3], and 250 ml H2O was refluxed 21.5 hr to give 76.5% 4,4-ethylenebis(1-benzoylsemicarbazide) [32304-03-3], m. 268-64.deg.. 4,4',4,4'-Diethylenebis-(1-benzoylsemicarbazide) [32251-24-4] was prepd. by refluxing a mixt. of 2-phenyl-.DELTA.2-1,3,4-oxadiazolin-5-one, piperazine [110-85-0] and H2O. 4,4'-Ethylenebis(semicarbazide hydrochloride) [**33618-20-1**] was polymd. with fumaroyl chloride [627-63-4] in 64%

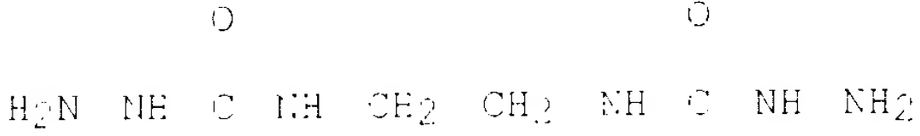
yield to give a copolymer, m. .leq.300. Styrene [100-42-5] was polymd. in the presence of N,N'-ethylenebis(2-cyano-2-propylazoformamide) (I) [32251-39-9] and the rate of polymn. at 5% and 10% conversion was 6.47 .tim. 10-3 and 6.27 .tim. 10-3 moles/l.-min resp., compared to 2.81 .tim. 10-3 moles/l.-min at both conversions in the absence of I.

IT **32239-91-1P 32251-26-6P 33618-20-1P**
**33636-52-1P 34777-39-4P**
RL: PREP (Preparation)
(prepn. of)

RN 32239-91-1 HCAPLUS
CN 2-Butenedioyl dichloride, (E)-, polymer with 2,2'-(1,2-ethanediyl)bis[hydrazinecarboxamide] (9CI) (CA INDEX NAME)

CM 1

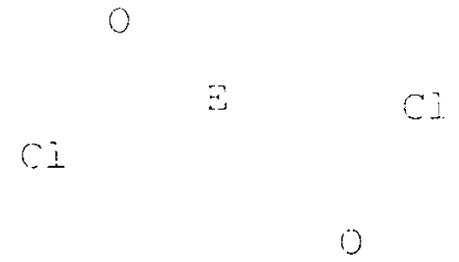
CRN 32251-26-6
CMF C4 H12 N6 O2



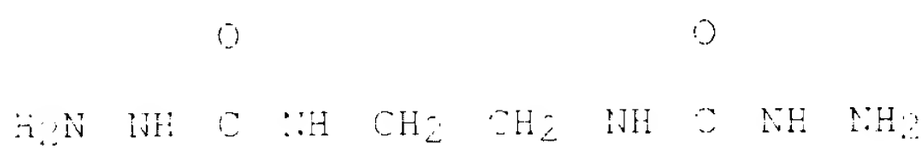
CM 2

CRN 627-63-4
CMF C4 H2 Cl2 O2

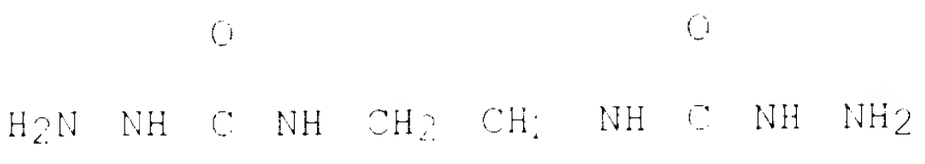
Double bond geometry as shown.

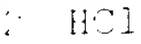


RN 32251-26-6 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)



RN 33618-20-1 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis-, dihydrochloride (9CI) (CA INDEX NAME)

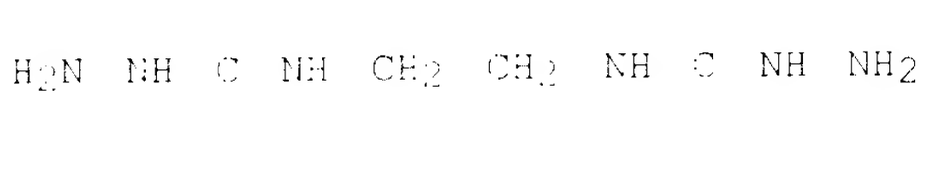




RN 33636-52-1 HCAPLUS
CN Carbonochloridic acid, 1,4-butanediyl ester, polymer with N,N'-1,2-ethanediylbis[hydrazinecarboxamide] (9CI) (CA INDEX NAME)

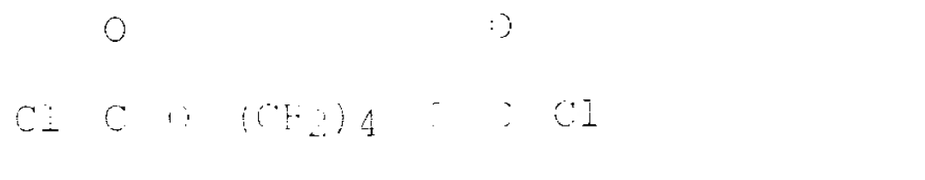
CM 1

CRN 33251-26-6
CMF C4 H12 N6 O2



CM 2

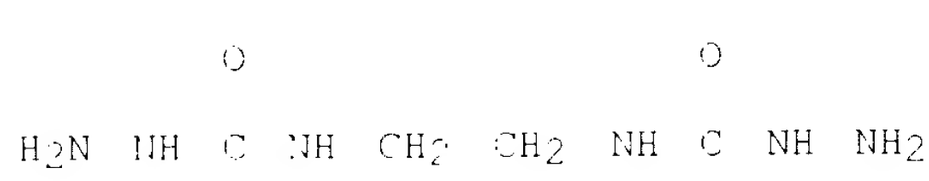
CRN 2157-16-6
CMF C6 H8 Cl2 O4



RN 34777-39-4 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis-, polymer with 2,2,4,4-tetramethyl-1,3-cyclobutanedione (9CI) (CA INDEX NAME)

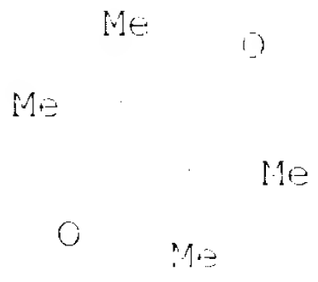
CM 1

CRN 33251-26-6
CMF C4 H12 N6 O2



CM 2

CRN 933-52-3
CMF C8 H12 O2



L9 ANSWER 25 OF 39 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:4063 HCAPLUS
DOCUMENT NUMBER: 80:4063
TITLE: 4,4'-Alkylenebis(semicarbazide) and derivatives
INVENTOR(S): Sheppard, Chester S.; Macleay, Ronald E.
PATENT ASSIGNEE(S): Pennwalt Corp.
SOURCE: U.S., 8 pp. Division of U.S. 3,565,200 (CA 75;77759k).
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3755443 | A | 19710828 | US 1970-58618 | 19700622 |
| US 3565200 | A | 19710223 | US 1966-556263 | 19660609 |

PRIORITY APPLN. INFO.: US 1966-556263 19660609

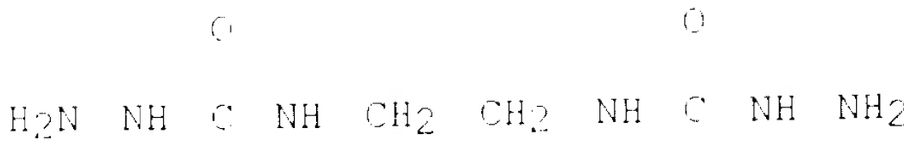
AB 4,4-Ethylenebis(semicarbazide) (I) [**32251-26-6**], 4,4'-ethylenebis(1-benzoylsemicarbazide) (II) [42304-03-3], 4,4'-ethylenebis(semicarbazide) dihydrochloride (III) [**33618-20-1**], BzNHNHCONH(CH2)12NHCONHNHBz, and 8 derivs. of I, such as (BzN:NCONHCH2)2, (Me2C:NNHCONHCH2)2, and (NCCMe2NHNHCONHCH2)2, are prepd. Also prepd. are the IV with R = BzNHNH, H2NNH (dihydrochloride), BzN:N, iso-PrOOCNHNH, iso-PrOOCN:N, and H2NCON:N. These compds. are used as monomers, polymn. catalysts, and blowing agents. Thus, 2-phenyl-.DELTA.2,1,3,4-oxadiazolin-5-one [1199-02-6] 50, ethylenediamine [107-15-3] 9, and water 150 g were refluxed for 11.5 hr to prep. 76.5% II and a minor amt. of 4-(.beta.-aminoethyl)-1-benzoylsemicarbazide. Refluxing of II (3 g) in 100 ml 10% HCl for 3 3/4 hr gave 1 g III which was dissolved in 10 ml water and treated with 0.64 g 50% aq. NaOH to prep. I. A polymer of I and fumaroyl chloride (IV) [627-63-4] was prepd. by adding 1.53 g IV in 25 ml toluene to a soln. of III 2.49, 50% NaOH 1.6, NaCl 1, and Na2CO3 1.59 g in 25 ml water. This polymer was heated at 230-50.deg., 20 mm for 2 hr to prep. a polyoxadiazole m. >300.deg.. Refluxing of III (0.8 g) and Na acetate (0.59 g) in 13 ml water with tetramethyl-1,3-cyclobutanedione (V) [933-52-8] gave a I-V polymer which did not melt or discolor to 305.deg..

IT **32239-91-1P 33618-20-1P 33636-52-1P**
**34777-39-4P**
RL: PREP (Preparation)
(prepn. of)

RN 32239-91-1 HCAPLUS
CN 2-Butenedioyl dichloride, (E)-, polymer with 2,2'-(1,2-ethanediyl)bis[hydrazinecarboxamide] (9CI) (CA INDEX NAME)

CM 1

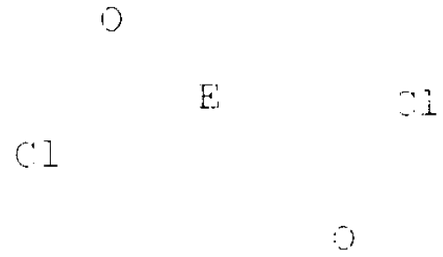
CRN 32251-26-6
CMF C4 H12 N6 O2



CM 2

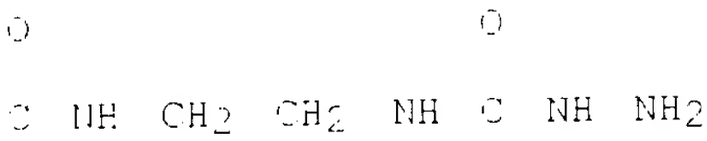
CRN 607-63-4
CMF C4 H2 Cl2 O2

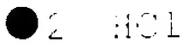
Double bond geometry as shown.





RN 3?613-..0-1 HCAPLUS
CN Hydraz.n.ecarboxamide, N,N'-1,2-ethanediylbis-, dihydrochloride (9CI) (CA INDEX NAME)

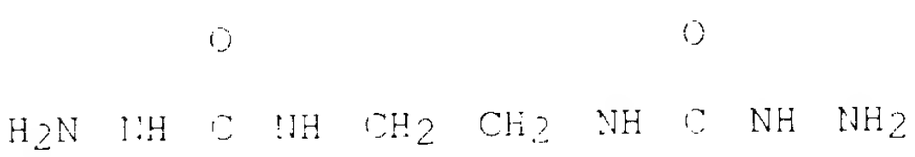




RN 33636-9?-1 HCAPLUS
CN Carbonochloridic acid, 1,4-butanediyl ester, polymer with N,N'-1,2-ethanediylbis[hydrazinecarboxamide] (9CI) (CA INDEX NAME)

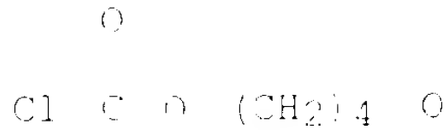
CM 1

CRN 32251-26-6
CMF C4 H12 N6 O2



CM 2

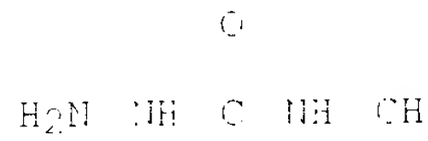
CRN 1157-16-?
CMF C6 H8 Cl2 O4



RN 34777-39-4 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis-, polymer with 2,2,4,4-tetramethyl-1,3-cyclobutanedione (9CI) (CA INDEX NAME)

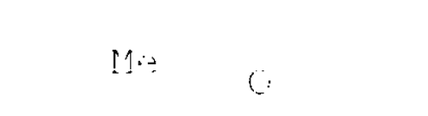
CM 1

CRN 32251-26-6
CMF C4 H12 N6 O2



CM 2

CRN 933-52-4
CMF C8 H12 O2



L9 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1971:477759 HCAPLUS
DOCUMENT NUMBER: 75:77759
TITLE: Alkylenebis(benzoylsemicarbazides)
INVENTOR(S): Sheppard, Chester S.; MacLeay, Ronald E.
PATENT ASSIGNEE(S): Pennwalt Corp.
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3552949 | A | 19710112 | US 1966-556263 | 19660609 |
| US 3755445 | A | 19730828 | US 1970-59808 | 19700622 |
| US 3755248 | A | 19730828 | US 1970-59807 | 19700622 |

PRIORITY APPLN. INFO.: US 1966-556263 19660609
GI For diagram(s), see printed CA Issue.
AB Alkylenebis(benzoylsemicarbazides), useful as intermediates in the prepn. of blowing agents and polymers, were prepd. by treating 2-substituted-.DELTA.2-1,3,4-oxadiazolin-5-ones with primary and secondary

diamines at 90-115.degree.. Thus, 5 g 2-phenyl-.DELTA.2-1,3,4-oxadiazolin-5-one and 3.0 g ethylenediamine was refluxed in 250 ml of water to give 4,4'-ethylenebis(1-benzoyl-semicarbazide) (I) m. 162-4.degree.. Similarly prepd. were 4,4',4,4'-diethylenebis(1-benzoylsemicarbazide) (II) and 4,4'-dodecamethylenebis(1-benzoylsemicarbazide). I was hydrolyzed with HCl and then treated with NaOH to yield 4,4'-ethylenebis(1-semicarbazide) which copolymd. interfacially with fumaroyl chloride to give poly(fumaroyliminoureylenoethylenemethylenimino) (III). On heating 2 hr at 130-50.degree./20 mm III yielded a polyoxadiazole. I.2HCl was treated with H2O, NaOAc and Me2CO to yield 4,4'-ethylenebis(1-isopropylidenesemicarbazide) which was treated with HCN to give ethylenebis[1-(2-cyano-2-propyl)-semicarbazide] (IV). IV was oxidized to N,N'-ethylenebis(2-cyano-2-propylazoformamide) which initiated the polymn. of styrene and was used as a blowing agent for vinyl foams.

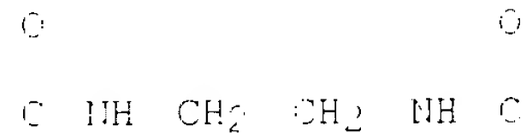
IT **32239-91-1P 32251-26-6P 33618-20-1P**
**33636-52-1P 34777-39-4P**
PL: PREP (Preparation)
(prepn. of)

RN 32239-91-1 HCAPLUS

CN 2-Butenedioyl dichloride, (E)-, polymer with 2,2'-(1,2-ethanediyl)bis[hydrazinecarboxamide] (9CI) (CA INDEX NAME)

CM 1

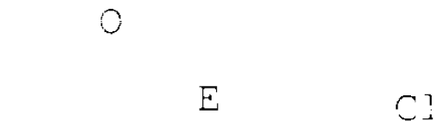
CRN 32251-26-6
CMF C4 H12 N6 O2



CM 2

CRN 627-63-4
CMF C4 H2 Cl2 O2

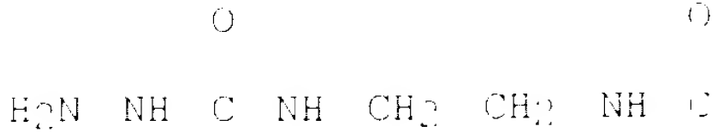
Double bond geometry as shown.



RN 32251-26-6 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)

RN 33618-20-1 HCAPLUS

CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis-, dihydrochloride (9CI) (CA INDEX NAME)

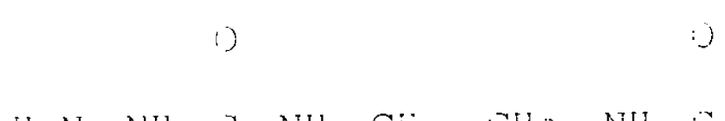


● 2 HCl

RN 33636-50-1 HCAPLUS
CN Carbonochloridic acid, 1,4-butanediyl ester, polymer with N,N'-1,2-ethanediylbis[hydrazinecarboxamide] (9CI) (CA INDEX NAME)

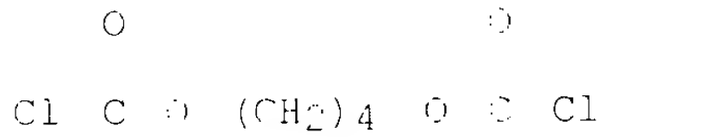
CM 1

CRN 22251-76-6
CMF C4 H12 N6 O2



CM 2

CRN 2157-16-6
CMF C6 H8 Cl2 O4



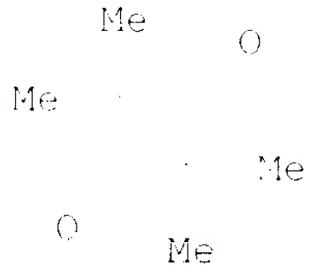
RN 94777-30-4 HCAPLUS
CN Hydrazinecarboxamide, N,N'-1,2-ethanediylbis-, polymer with 2,2,4,4-tetramethyl-1,3-cyclobutanedione (9CI) (CA INDEX NAME)

CM 1

CRN 22251-76-6
CMF C4 H12 N6 O2

CM 2

CRN 933-52-3
CMF C8 H12 O2



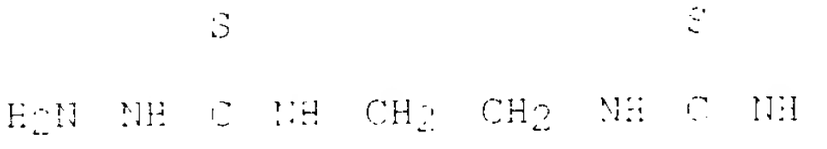
L9 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:70686 HCAPLUS
DOCUMENT NUMBER: 55:70686
ORIGINAL REFERENCE NO.: 55:13431d-i,13432a-b
TITLE: Nitro olefins. II. Derivatives of .alpha.-nitrostyrophenone
AUTHOR(S): Campbell, Richard D.; Schultz, Frederick J.
CORPORATE SOURCE: State Univ. of Iowa, Iowa City
SOURCE: Journal of Organic Chemistry (1960), 25, 1877-81
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 54, 15591a. Reactions for the prepn. of derivs. of PhCOCH2NO2 (I) gave a series of 16 related compds. and the ultraviolet and infrared spectra were reported and discussed. I (8.35 g.) in 60 ml. dry C6H6 stirred with dropwise addn. of 25 g. KOH in 40 ml. abs MeOH and the product washed twice with 1:1 MeOH-C6H6 yielded 76% vacuum-dried PhC(OK):CHNO2. Similarly were prepd. PhC(OHH4):CHNO2 and PhC(OZ):CHNO2 (Z = morpholinium). The prepn. of .alpha.-amino-.beta.-nitrostyrenes was accomplished by treatment of PhCOCl:CHNO2 (II) with appropriate amines. PhC.tplbond.CH (10 g.) in 75 ml. cold dry Et2O treated with 15 g. liquid NOCl, the mixt. kept 10 days with gradually rising temp. and gas evolution, the pale orange liquid evapd., and the yellow oil distd. gave 16.5 g. II, m. 5-6.degree. (petr. ether), strongly lachrimatory. Et2O (75 ml.) in a heavy-wall tube cooled to -80.degree. (solid CO2-Me2CO) and bubbled through with adsorption of 15 g. NOCl, stirred with gradual addn. of 17 g. PhC.tplbond.CH and kept 2 days at -30.degree. and 7 days at 20.degree., the solvent removed in vacuo and the residue distd. gave a yellow oil, b2.0 103.9.degree., crystd. from petr. ether to yield 35.8% II. Freshly distd. morpholine (0.19 g.) added to 1 g. II and the Et2O-sol., H2O-insol. portion crystd. from ligroine (b. 60-70.degree.) yielded 47.5% .alpha.-morpholino-.beta.-nitrostyrene, m. 167-9.degree.. Under similar conditions with 2-hr. reflux of the mixt., BrNH2 and II yielded 91.7% PhC(NHPh):CHNO2, m. 123-4.degree., and PhCH2NH2 gave 86.8% PhC(NHCH2Ph):CHNO2, m. 91.5degree. (CCl4). II and cyclohexylamine kept 16 hrs. yielded 65% PhC(NHC6H11):CHNO2, m. 113-14.degree. (Et2O). The structures of these amine reaction products were established by acid hydrolysis to I. Several attempts were made to prep. .alpha.-acyloxy-.beta.-nitrostyrenes by acylation of I. I (4.1 g.) and 3,5-(O2N)2C6H3COCl (from 8 g. 3,5-(O2N)2C6H3CO2H) refluxed 2 hrs. in 2 ml. dry C5H5N and the warm soln. filtered gave 77.4% PhC[3,5-(O2N)2C6H3CO2]:CHNO2 (III), m. 187-8.degree.. III (2.0 g.) and 25 ml. 10% NaOH warmed 2 hrs. on a steam bath and the cold soln. acidified at 0.degree. with 6M HCl, extd. with Et2O and a portion of the dried ext. chromatographed showed the presence of MeNO2. Similar acylation of I with p-O2NC6H4COCl yielded 61% PhC(4-O2NC6H4CO2):CHNO2, m. 168-7.degree. (Me2CO, CHCl3-petr. ether). Addnl. products were obtained in a homologous series by reaction with PhCH:CMeNO2 (IV) and PhCHBrCMeBrNO2. Previously were prepd. homologs PhCH:CBrNO2 and PhCHBrCHBrNO2. IV (1 g.) in 15 ml. freshly distd.

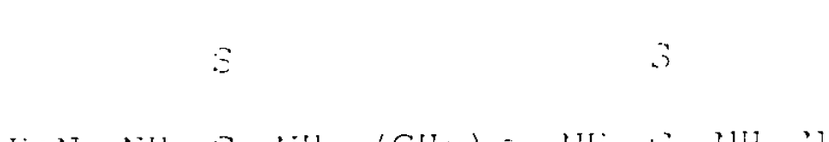
morpholine kept 16 hrs. on a steam bath and the cooled soln. dild. with Et2O, washed (H2O) and evapd., the residue taken up in hot ligroine (b. 66-70.degree.) and the decolorized soln. cooled yielded 39.2% 1-phenyl-1-morpholino-2-nitropropane, m. 142-4.degree. (petr. ether). I (0.1 mole) in 175 ml. dry CH2Cl2 refluxed 4 days with 0.1 mole PCl5 and the residue vacuum distd. at 90.degree./12 mm., extd. with ligroine and the product recrystd. yielded 22.3% PhCCl:C(NO2)Ph, m. 90.degree.. Spectral patterns resulting from keto-enol equil., H chelation, dipole interaction, and **conjugation** effects were discussed.

IT **1728-65-0**, Semicarbazide, 4,4'-ethylenebis[3-thio-
**56473-15-5**, Semicarbazide, 4,4'-hexamethylenebis[3-thio-
(prepn. of)

RN 1728-65-0 HCAPLUS
CN Hydrazinecarbothioamide, N,N'-1,2-ethanediylbis- (9CI) (CA INDEX NAME)



RN 56473-15-5 HCAPLUS
CN Hydrazinecarbothioamide, N,N'-1,6-hexanediylbis- (9CI) (CA INDEX NAME)



L9 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1956:91004 HCAPLUS
DOCUMENT NUMBER: 50:91004
ORIGINAL REFERENCE NO.: 50:17123g-i,17124a
TITLE: The inhibition of growth of sarcoma 180 by combinations of vitamin B6 antagonists and acid hydrazides
AUTHOR(S): Brockman, R. Wallace; Thomson, J. Richard; Schabel, Frank M., Jr.; Skipper, Howard E.
CORPORATE SOURCE: Southern Research Inst., Birmingham, AL
SOURCE: Cancer Research (1956), 16, 788-95
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

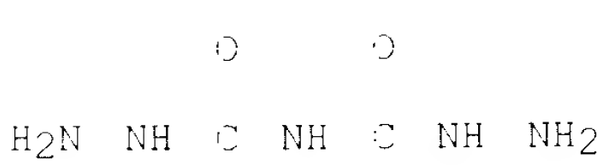
AB Deoxypyridoxine-HCl (I) and deoxypyridoxine phosphate (II) significantly restricted growth of sarcoma 180 in mice on a diet deficient in vitamin B6 (III), but not in mice on a complete diet. Many compds. of the acid hydrazide type also restricted growth of the sarcoma on a diet deficient in III, but none except 1,5-diaminobiuret at high dosage levels affected the tumor in mice on a complete diet. Combinations of II with acid hydrazides were more inhibitory to the tumor in mice on a complete diet than were combinations of I with acid hydrazides. The same combinations given to mice deficient in III resulted in severe restriction of tumor growth. Vitamins of the III group, i.e., pyridoxine-HCl, pyridoxamine-HCl, pyridoxal-HCl, and pyridoxal phosphate (IV), almost completely prevented the tumor-inhibiting effect of the combinations. Spectrophotometric studies demonstrated ability of the representative acid hydrazides to react with IV. The observed ability of acid hydrazides to enhance the inhibition of sarcoma 180 produced by III-deficiency and

III-antagonists is attributed to formation of an inactive **conjugate** between the acid hydrazides and IV.

IT **4375-11-5,** Imidodicarboxylic acid, dihydrazide
(effect on sarcoma)

RN 4375-11-5 HCAPLUS

CN Imidodicarbonic dihydrazide (9CI) (CA INDEX NAME)



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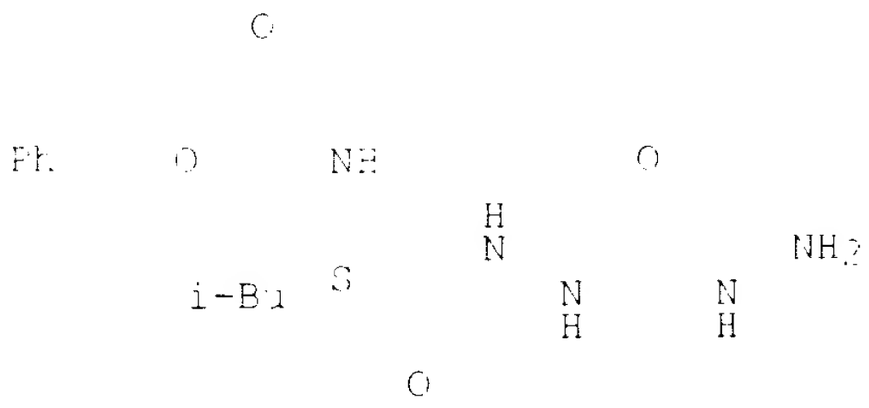
L14 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:461867 HCAPLUS
DOCUMENT NUMBER: 137:166345
TITLE: Inhibition of Cathepsin K with Lysosomotropic Macromolecular Inhibitors
AUTHOR(S): Wang, Dong; Bechar, Michal; Li, Weijie; Kopeckova, Pavla; Bromme, Dieter; Kopecek, Jindrich
CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry/CCCD and Department of Bioengineering, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Biochemistry (2002), 41(28), 8849-8859
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cathepsin K is the major enzyme responsible for the degrdn. of the protein matrix of bone and probably for the destruction of articular cartilage in rheumatoid arthritis joints. These processes occur mainly in the resorption lacuna and within the lysosomal compartment. Here, we have designed, synthesized, and evaluated new lysosomotropic (water-sol.) polymer-cathepsin K inhibitor **conjugates**. In particular, we characterized the relationship between **conjugate** structures and their activity to inhibit cathepsins K, B, L, and papain. A potent selective cathepsin K inhibitor, 1,5-bis(N-benzyloxycarbonylleucyl)carbohydrazide, was modified to 1-(N-benzyloxycarbonylleucyl)-5-(phenylalanylleucyl)carbohydrazide (I) to facilitate polymer **conjugation**. It was **conjugated** to the polymer chain termini of two water-sol. polymers (.alpha.-methoxy poly(ethylene glycol), abbreviated as mPEG-I; semitelechelic poly[N-(2-hydroxypropyl)methacrylamide], abbreviated as ST-PHPMA-I). The **conjugation** of inhibitor I to N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer side chains was accomplished via either a Gly-Gly spacer (PHPMA-GG-I) or with no spacer between I and the copolymer backbone (PHPMA-I). Kinetic anal. revealed that free inhibitor I possessed an apparent second-order rate const. against cathepsin K (kobs/[I] = 1.3.times.106 M-1 s-1) similar to that of unmodified 1,5-bis(Cbz-Leu) carbohydrazide, while I **conjugated** to the chain termini of mPEG and ST-PHPMA-COOH had slightly lower values (about 8.times.105 M-1 s-1). The kobs/[I] values for I attached to the side chains of HPMA copolymers (PHPMA-GG-I and PHPMA-I) were about 3.times.104 M-1 s-1. When tested against cathepsin L, inhibitor I and all its polymer **conjugates** produced kobs/[I] values 1-2 orders of magnitude less than those detd. for cathepsin K, while for cathepsin B and papain, the values were 2-4 orders of magnitude lower. The ability of mPEG-I and ST-PHPMA-I to inhibit cathepsin K activity in synovial fibroblasts was also evaluated. Both polymer-bound inhibitors were internalized by endocytosis and were ultimately trafficked to the lysosomal compartment. ST-PHPMA-I was internalized faster than mPEG-I. The inhibitory activity in the synovial fibroblast assay correlated with the rate of internalization.
IT **190142-08-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(inhibition of human lysosome cathepsin K with lysosomotropic macromol. inhibitors)
RN 190142-08-6 HCAPLUS
CN L-Leucine, N-[(phenylmethoxy)carbonyl]-, 2-(hydrazinocarbonyl)hydrazide (9CI) (CA INDEX NAME)

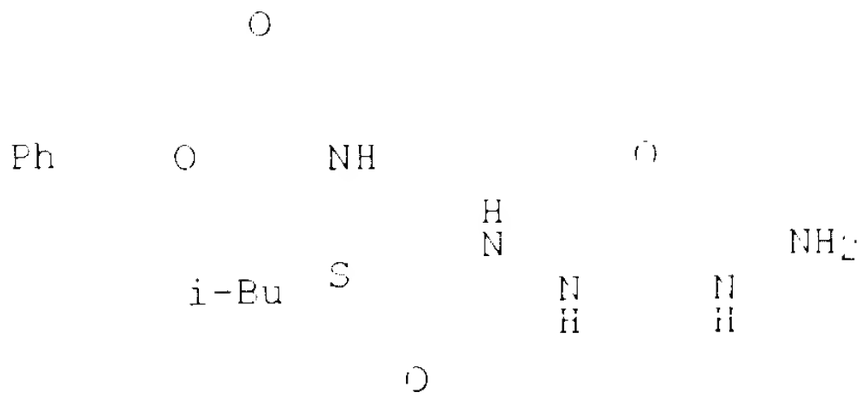
Absolute stereochemistry.



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:350632 HCAPLUS
DOCUMENT NUMBER: 138:112178
TITLE: Design and synthesis of cathepsin K inhibitor-polymer **conjugates**
AUTHOR(S): Bechar, M.; Wang, D.; Kopeckova, P.; Kopecek, J.
CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 2, 1319-1320. Controlled Release Society: Minneapolis, Minn.
CODEN: 69CNY8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A carbohydrazide based cathepsin K inhibitor was synthesized and **conjugated** with water-sol. polymers. The enzyme inhibition activities of the low mol. wt. and macromol. inhibitors were tested with papain, a model cysteine protease. The **conjugates** have the potential to facilitate delivery of the inhibitor into the bone resorption lacuna.
IT **190142-08-6DP**, reaction products with polyhydroxypropylmethacrylamides
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design and synthesis of cathepsin K inhibitor-polymer **conjugates**)
RN 190142-08-6 HCAPLUS
CN L-Leucine, N-[(phenylmethoxy)carbonyl]-, 2-(hydrazinocarbonyl)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:684457 HCAPLUS
DOCUMENT NUMBER: 129:290447
TITLE: Preparation of branched hydrazone linkers for therapeutic drugs
INVENTOR(S): King, Dalton; Firestone, Raymond A.; Trail, Pamela
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 37 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

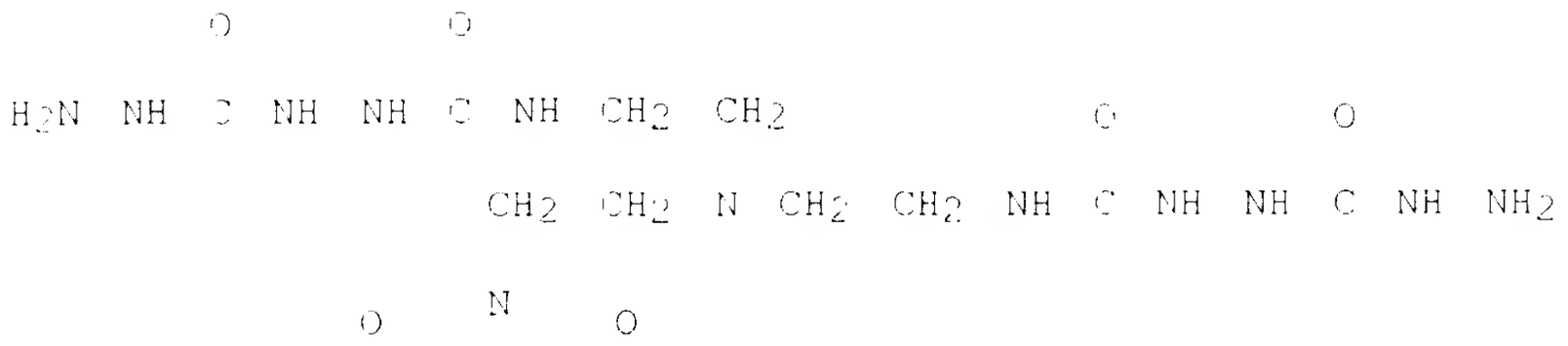
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5814805 | A | 19981020 | US 1996-770614 | 19961219 |
| US 6511101 | B1 | 20030128 | US 1998-136351 | 19980819 |

PRIORITY APPLN. INFO.: US 1995-9100P P 19951222
US 1996-770614 A3 19961219

AB Branched linkers A-Q-CONHCH[(NH)bCO-Wm-X](CH2)a(NH)bCO-(W)m-X [A is a thiol acceptor, Q is a bridging group, b and m are integers 0 or 1, W is a spacer moiety, a is an integer 2, 3, or 4, X is NHNH2, NHNHCONHNH2, or NHCH[(NH)bCO-Wm-X1](CH2)a(NH)bCO-(W)m-X1, where W, a, b and are as defined, X1 is NHNH2, NHNHCONHNH2, or NHCH[(NH)bCO-Wm-X2](CH2)a(NH)bCO-(W)m-X2, where W, a, b and are as defined, X2 is NHNH2, NHNHCONHNH2, or NHCH[(NH)bCO-Wm-X3](CH2)a(NH)bCO-(W)m-X3, where W, a, b and are as defined, X3 is NHNH2, NHNHCONHNH2, or NHCH[(NH)bCO-Wm-X4](CH2)a(NH)bCO-(W)m-X4, where W, a, b and are as defined, X4 is NHNH2, NHNHCONHNH2] were prepd. for linking a targeting ligand such as an antibody to a therapeutically active drug. Thus, the maleimidobutyrylglutamyldihydrazone of doxorubicin was prepd. and assayed for antitumor activity.

IT **192874-02-5P**
RL: BCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of branched hydrazone linkers for therapeutic drugs)

RN 192874-02-5 HCAPLUS
CN 2,8,5,8,11,13,14-Heptaazapentadecanedioic acid, 8-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]-4,12-dioxo-, dihydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 110 THERE ARE 110 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:503560 HCAPLUS
DOCUMENT NUMBER: 127:136079
TITLE: Preparation of branched hydrazone linkers for linking antibodies to therapeutic drugs
INVENTOR(S): King, Dalton; Firestone, Raymond; Trail, Pamela
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9723243 | A1 | 19970703 | WO 1996-US20513 | 19961217 |
| W: CA, JP, MX | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 871490 | A1 | 19981014 | EP 1996-944522 | 19961217 |
| EP 871490 | B1 | 20030319 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2000503639 | T2 | 20000328 | JP 1997-523841 | 19961217 |
| AT 234635 | E | 20030415 | AT 1996-944522 | 19961217 |

PRIORITY APPLN. INFO.: US 1995-9100P P 19951222
WO 1996-US20513 W 19961217

OTHER SOURCE(S): MARPAT 127:136079
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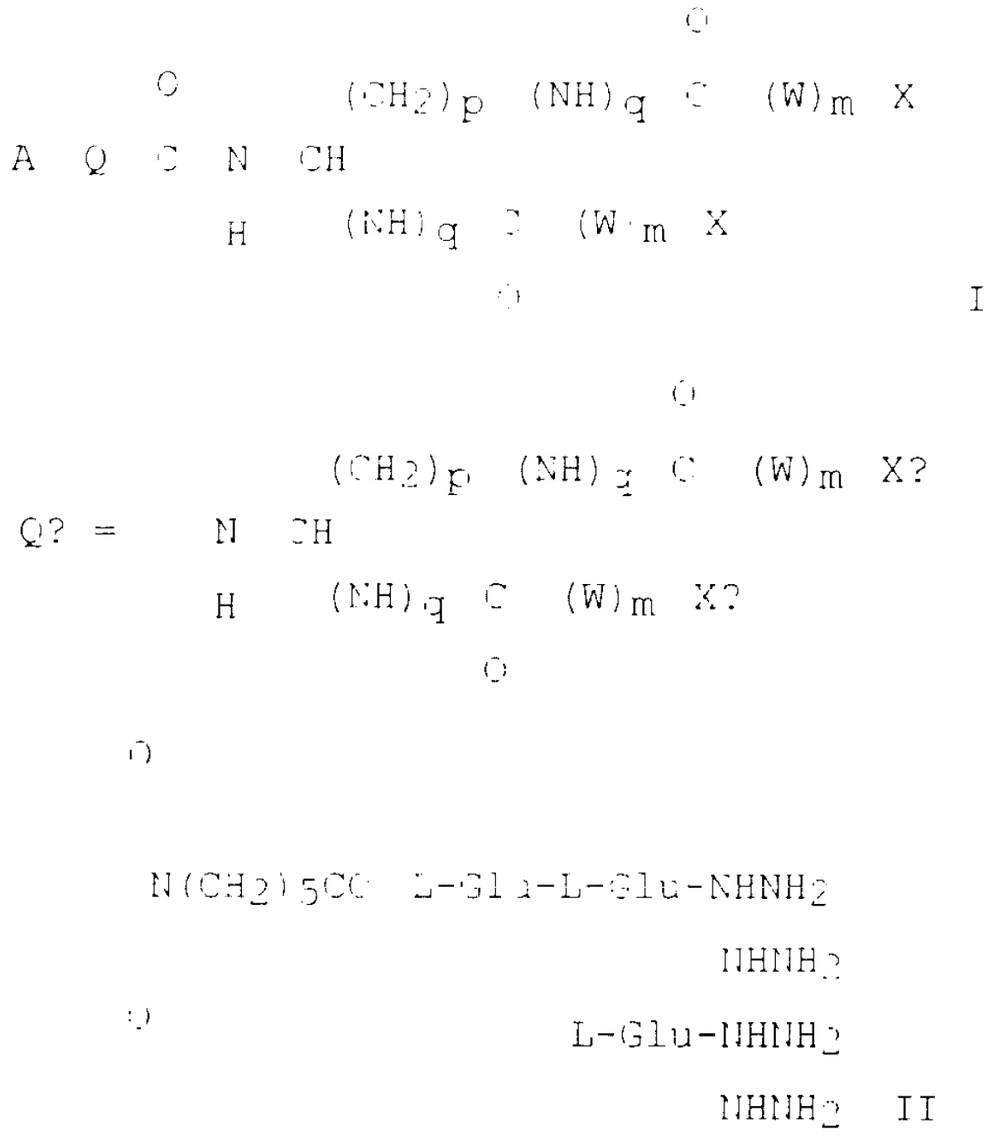
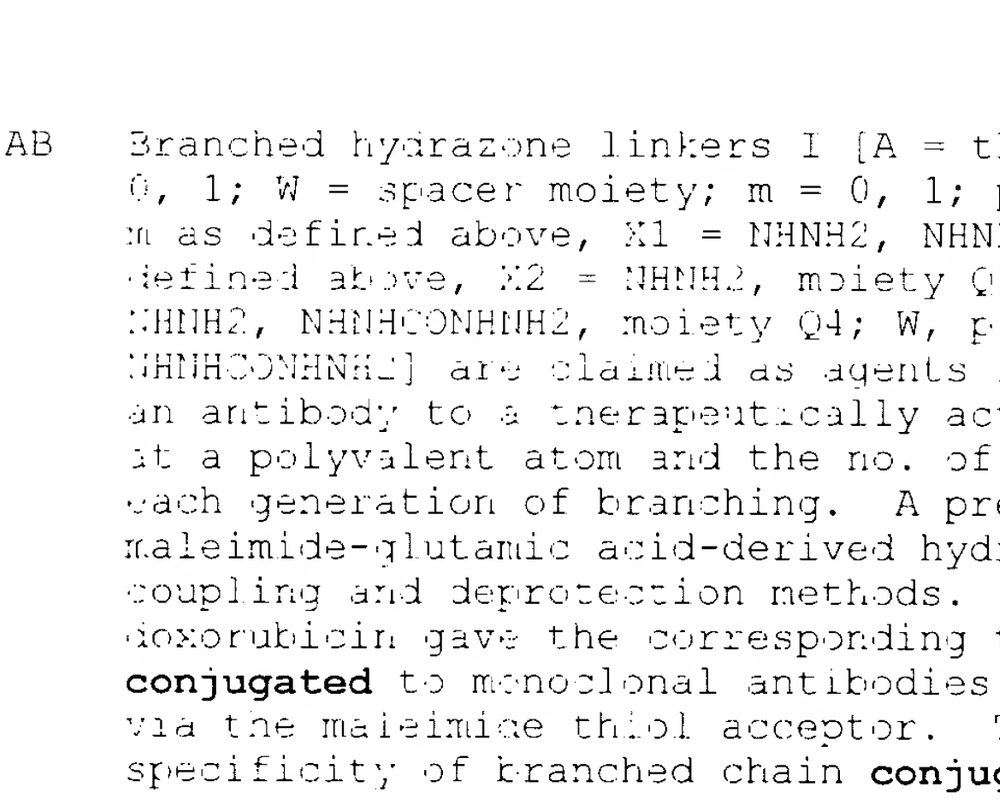




AB Branched hydrazone linkers I [A = thiol acceptor; Q = bridging group; q = 0, 1; W = spacer moiety; m = 0, 1; p = 2-4; X = NHNH2, moiety Q1; W, p, q, m as defined above, X1 = NHNH2, NHNHCONHNH2, moiety Q2; W, p, q, m as defined above, X2 = NHNH2, moiety Q3; W, p, q, m as defined above, X3 = NHNH2, NHNHCONHNH2, moiety Q4; W, p, q, m as defined above, X4 = NHNH2, NHNHCONHNH2] are claimed as agents for linking a targeting ligand such as an antibody to a therapeutically active drug. The point of branching is at a polyvalent atom and the no. of drugs increases by a factor of two for each generation of branching. A preferred drug is doxorubicin. Thus, maleimide-glutamic acid-derived hydrazone linker II was prepd. by std. coupling and deprotection methods. Condensation of II with 4 equiv of doxorubicin gave the corresponding tetrakis(hydrazone), which was then **conjugated** to monoclonal antibodies and **immunoconjugates** via the maleimide thiol acceptor. The in vivo antitumor potency and specificity of branched chain **conjugates** II and related mols. were detd.

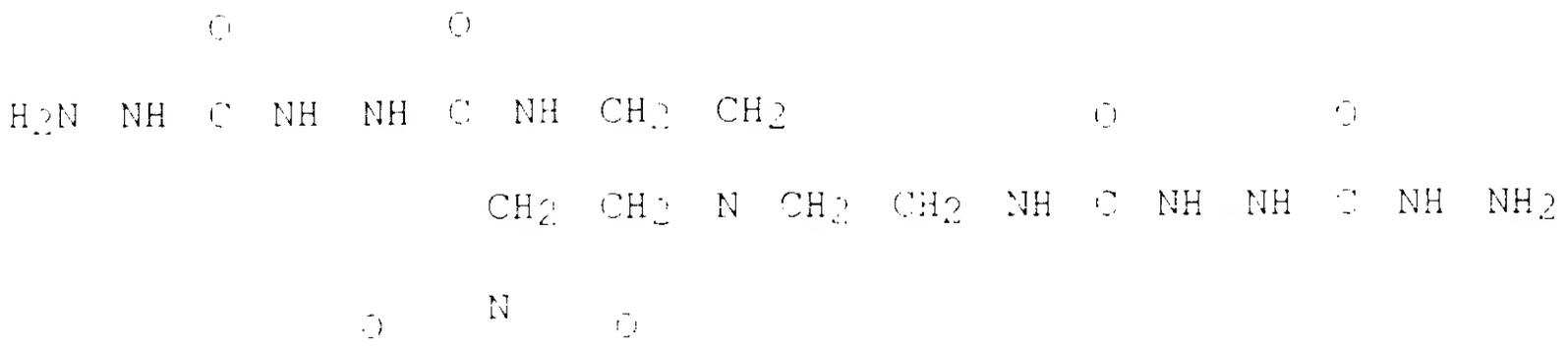
IT **192874-02-5P**

PL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

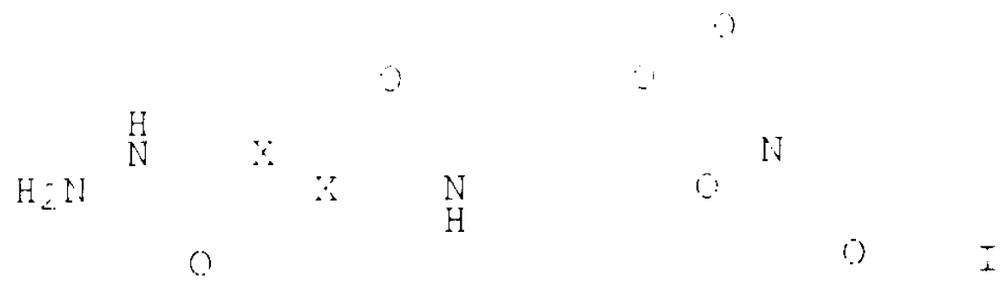
(prepn. of branched hydrazone linkers for linking antibodies to therapeutic drugs)

RN 192874-02-5 HCAPLUS

CN 2,5,8,11,13,14-Heptaazapentadecanedioic acid, 8-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]-4,12-dioxo-, dihydrazide (9CI) (CA INDEX NAME)



L14 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:466519 HCAPLUS
DOCUMENT NUMBER: 125:221494
TITLE: Synthesis of reagents for the one step incorporation of hydrazide functionality onto the lysine residues of proteins, and their use as linkers for carbonyl containing molecules
AUTHOR(S): Scott, William L.; Cwi, Cynthia
CORPORATE SOURCE: Lilly Research Laboratories, Technology Core Research, Indianapolis, IN, 46285, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(13), 1491-1496
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



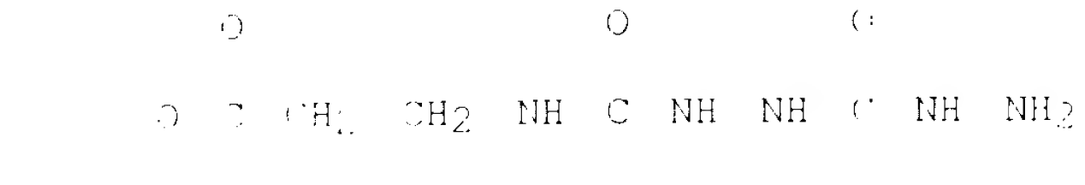
AB Two new reagents I.CF3CO2H (X = CH2, NH) were prepd. for the one step incorporation of hydrazide functionalities onto lysine side chains in proteins. Their utility as linking reagents was demonstrated by their use in the coupling of two model aldehydes and the anticancer agent doxorubicin to a monoclonal antibody.

IT **181638-49-3P 181638-56-2DP**, C-terminal amides with lysine side chains in monoclonal antibody CC49
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **bifunctional** reagents for incorporation of hydrazide functionalities on protein lysine residues and use as linkers for carbonyl contg. mols.)

RN 181638-49-3 HCAPLUS
CN Carbonic dihydrazide, 2-[[[3-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3-oxopropyl]amino]carbonyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 181639-49-2
CMF C9 H14 N6 O6



CM 4

CRN 76-05-1
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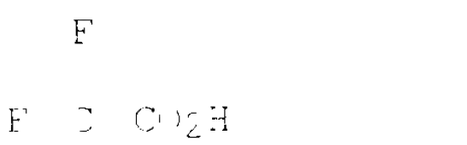
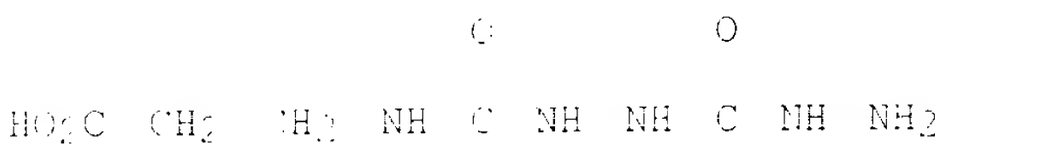


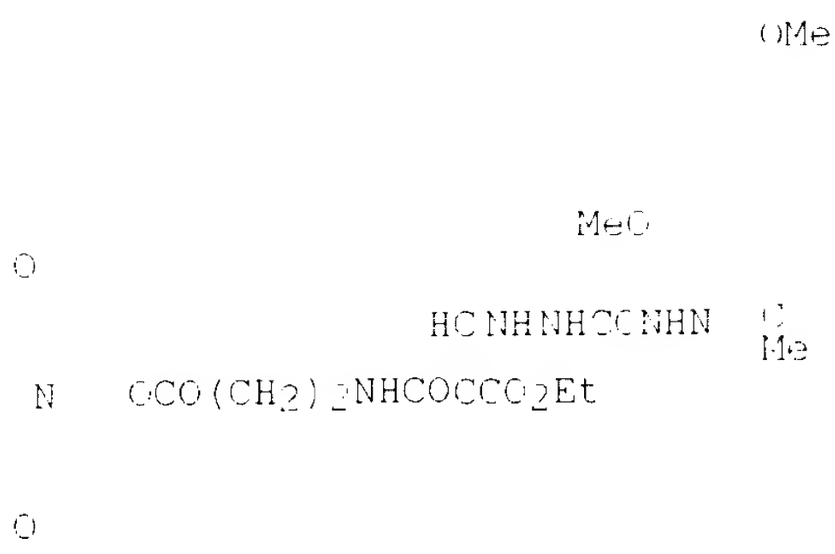
RN 181639-56-2 HCAPLUS
CN .beta.-Alanine, N-[[2-(hydrazinocarbonyl)hydrazino]carbonyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:257887 HCAPLUS
DOCUMENT NUMBER: 122:38822
TITLE: Antibody-drug **conjugates**
INVENTOR(S): Barton, Russell Lavern; Briggs, Stephen Lyle
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 6[illegible]4 | A1 | 19941102 | EP 1994-302952 | 19940425 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| JP 07 00895 | A2 | 19950106 | JP 1994-82952 | 19940421 |
| CA 2121990 | AA | 19941029 | CA 1994-2121990 | 19940422 |

PRIORITY APPLN. INFO.: US 1993-54704 19930428
OTHER SOURCE(S): MARPAT 122:38822
GI



I

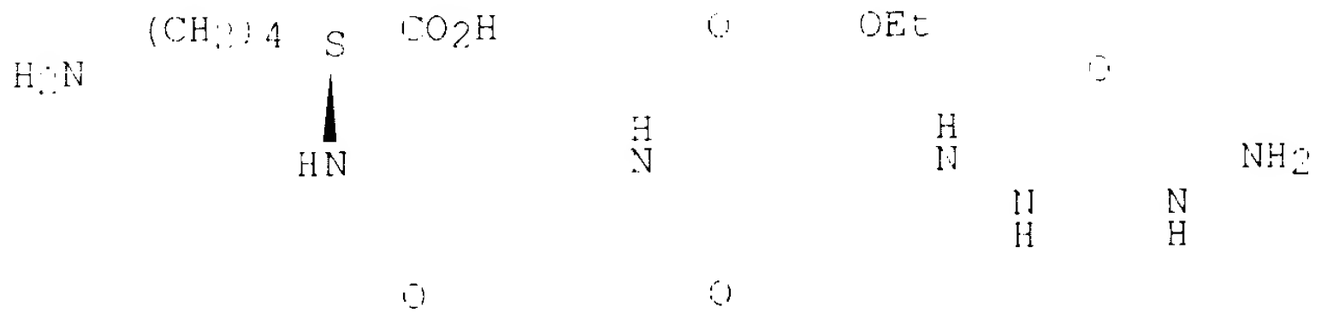
AB Malonate derivs. useful as linkers for prepn. of **immunoconjugates** comprising drugs and antibodies are provided. I was prepd. from Et malonate and .beta.-alanine benzyl ester by 6 steps and reacted with CC49 monoclonal antibody, then with doxorubicin in DMF to give an **immunoconjugate**.

IT **159795-68-3DP**, reaction products with antibody and doxorubicin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antibody-drug **conjugates**)

RN 159795-68-3 HCAPLUS

CN L-Lysine, N2-[N-[2-(ethoxycarbonyl)-3-[2-(hydrazinocarbonyl)hydrazino]-1-oxo-2-propenyl]-.beta.-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



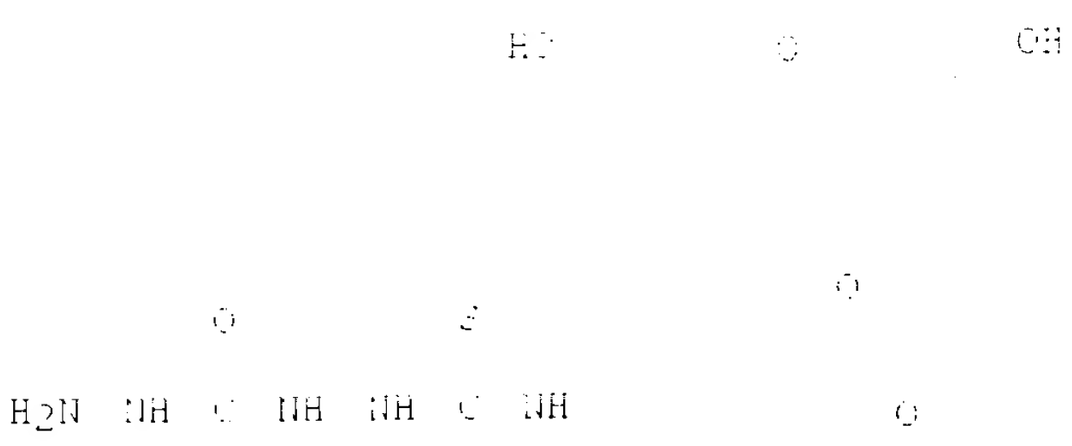
L14 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:573214 HCAPLUS
DOCUMENT NUMBER: 121:173214
TITLE: Effect of derivatization of ribophosphate backbone and terminal ribophosphate groups in oligoribonucleotides on their stability and interaction with eukaryotic cells
AUTHOR(S): Boutorine, A. S.; Venyaminova, A. G.; Repkova, M. N.; Sergueyeva, Z. A.; Pyshnyi, D. V.
CORPORATE SOURCE: Sib. Div., Inst. Biorg. Chem., Novosibirsk, 630090, Russia
SOURCE: Biochimie (1994), 76(1), 23-32
CODEN: BIOMBE; ISSN: 0300-9084
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Various derivs. of oligoribonucleotides were synthesized by the H-phosphonate method. Different modifications of the ribophosphate

backbone were designed in order to protect the derivs. against nucleolytic enzymes present in the biol. media. These modifications include coupling of fluorescein moiety to 3'-terminal ribose, 2'-O-methylation of ribose, introduction of phosphoroamidates and coupling of the last 3'-terminal nucleotide via the 3'-3'-phosphodiester bond. All modifications were tested for their effect on the stability of the derivs. against phosphodiesterase from snake venom and nucleases of the cell culture media. 2'-O-methylated oligoribonucleotides contg. either terminal 3'-3'-linkage or two 3'-terminal phosphoroamidate internucleotide bonds appeared to be the most stable under the most severe conditions used. The results demonstrate a possibility to use protected oligoribonucleotide derivs. for expts. in vivo when the use of deoxy-analogs might be ineffective. The uptake of 2'-O-methylated derivs. and their 3'-cholesterol **conjugates** (coupled via a disulfide bond) by human carcinoma cells did not differ from that of the corresponding oligodeoxyribonucleotides. 95% of the bound derivs. were found in the membrane-cytosolic fraction, while only 15% were found in the nuclear fraction. The oligonucleotide moiety of 2'-O-methyloligoribonucleotide-cholesterol **conjugate** was not translocated through the cellular membrane. After cleavage of the linkage between cholesterol and oligonucleotide by dithiothreitol the major portion of the oligonucleotide moiety was released into the media. The derivs., as well as their 3'-cholesterol **conjugates**, which entered the cells, were stable and protected from action of dithiothreitol dissolved in culture media. These results demonstrate an endocytosis mechanism of penetration as obsd. in similar expts. using oligodeoxyribonucleotides.

IT **157597-83-6**
PL: PCT (Reactant); PACT (Reactant or reagent)
(reaction of, with oligoribonucleotide)

RN 157597-83-6 HCAPLUS

CN Carbonic dihydrazide, 2-[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]- (9CI) (CA INDEX NAME)



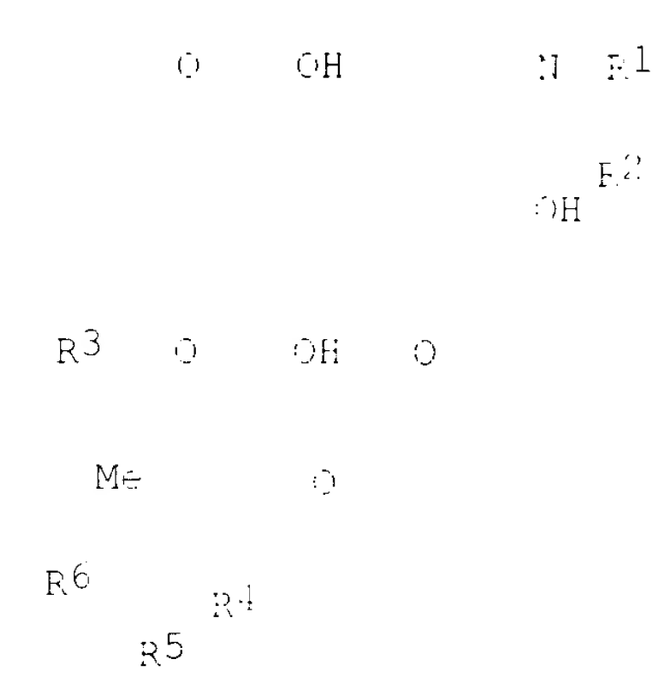
L14 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:214841 HCAPLUS
DOCUMENT NUMBER: 116:214841
TITLE: Preparation of anthracycline **immunoconjugates** as neoplasm inhibitors
INVENTOR(S): Kaneko, Takushi; Willner, David; Monkovic, Ivo; Greenfield, Robert S.; Braslawsky, Gary R.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 457[illegible] | A2 | 19911121 | EP 1991-107737 | 19910513 |
| EP 457[illegible] | A3 | 19920701 | | |
| EP 457[illegible] | B1 | 19960724 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| US 5137877 | A | 19920811 | US 1990-522996 | 19900514 |
| US 5137877 | B1 | 19960130 | | |
| AU 9174168 | A1 | 19911114 | AU 1991-74168 | 19910403 |
| AU 644651 | B2 | 19940310 | | |
| FI 9101989 | A | 19911115 | FI 1991-2189 | 19910510 |
| JP 04356795 | A2 | 19921210 | JP 1991-144757 | 19910513 |
| JP 3010811 | B2 | 20000221 | | |
| ZA 9103591 | A | 19920226 | ZA 1991-3591 | 19910513 |
| AT 138141 | E | 19960715 | AT 1991-107737 | 19910513 |
| ES 2087611 | T3 | 19960916 | ES 1991-107737 | 19910513 |
| CA 2042503 | AA | 19911115 | CA 1991-2042503 | 19910514 |
| CA 2042503 | C | 20020723 | | |
| US 5[illegible] | A | 19940802 | US 1992-[illegible] | 19920403 |
| JP 2000026404 | A2 | 20000125 | JP 1999-112583 | 19990519 |
| JP [illegible] | B2 | 20011204 | | |

PRIORITY APPLN. INFO.: US 1990-522996 A 19900514
JP 1991-144757 A3 19910513

OTHER SOURCE(S): MARPAT 116:214841

GI



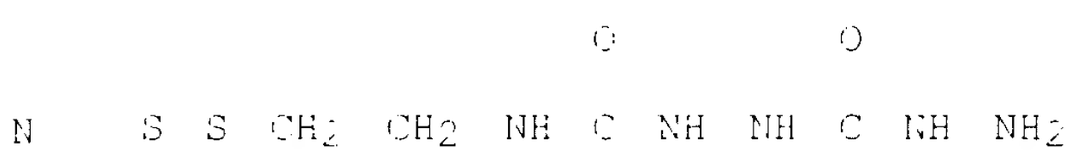
AB Antnracycline derivs. I [R1 = NHCONH(CH2)nSSR8, NHCONHNHCONH(CH2)nSSR8, NHCSNH(CH2)mCH:CH(CH2)nSSR8, NHCO2(CH2)nSSR8, NHArCONH(CH2)nSSR8, etc.; m, n = 1-10; R8 = (substituted) 2-pyridyl, -phenyl; Ar = phenylene; R2 = Me, CH2OH, CH2OCO(CH2)3Me, CH2OCOCH(OEt)2; R3 = OMe, OH, H; R4 = NH2 NHCOCF3, 4-morpholinyl, 3-cyano-4-morpholinyl, 1-piperidinyl, NHCH2Ph, N(CH2Ph)2, etc.; R5 = OH, tetrahydropyranyloxy, H; R6 = OH, H; R6 .noteq. OH when R5 = OH or tetrahydropyranyloxy], related compds., and their **conjugates** with ligands and antibodies, were prepd. Thus, 1-amino-4-[(2-pyridinyl)dithio]-2-butene-HCl (prepn. given) was treated with di(2-pyridyl) thiocarbonate and the product formed was condensed with MeO2CNHNH2. Deprotection of the resulting product by CF3CO2H gave N-[4-(2-pyridinyl)dithio]-2-butenyl]hydrazinecarbothioamide. This was condensed with adriamycin-HCl to give adriamycin 13-N-4-[(2-

pyridinyl)dithio]-2-butenylhydrazinecarbothioamide thiosemicarbazone.cntdot.HCl (II). The **immunoconjugate** of II with thiolated monoclonal antibody 5E9 had IC50 of 3.0 .times. 10-7M against Burkitt's lymphoma cells.

IT **133701-19-6P**
BL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for anticancer **immunoconjugates**)

RN 133701-19-6 HCAPLUS

CN Carbonic dihydrazide, 2-[[[2-(2-pyridinyldithio)ethyl]amino]carbonyl]-, monohydrochloride (CA INDEX NAME)



L14 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:436407 HCAPLUS
DOCUMENT NUMBER: 115:25407
TITLE: Novel trifunctional carrier molecule for the fluorescent labeling of haptens
AUTHOR(S): Bredehorst, Reinhard; Wemhoff, Gregory A.; Kusterbeck, Anne W.; Charles, Paul T.; Thompson, Richard B.; Ligler, Frances S.; Vogel, Carl Wilhelm
CORPORATE SOURCE: Dep. Biochem. Mol. Biol., Georgetown Univ., Washington, DC, 20007, USA
SOURCE: Analytical Biochemistry (1991), 193(2), 272-9
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors developed a novel trifunctional carrier mol. for the synthesis of hapten-fluorophore **conjugates** as reporter mols. in immunoassays. This carrier eliminates some of the disadvantages assocd. with currently used fluorophore-labeling procedures including high nonspecific binding. The backbone of the carrier consists of the 21 amino acid residues of the insulin A-chain mol. This polypeptide provides a single site (terminal amino group) for covalent coupling of the hapten, three carboxyl groups for the attachment of fluorophores, and four sulfhydryl groups for derivatization with hydrophilic residues to compensate for the hydrophobic effect of the attached fluorophores. The sites for fluorophore attachment are 4, 17, and 21 amino acids away from the hapten attachment site. This spatial sepn. minimizes quenching of the fluorescence signal due to interaction of the fluorophores with each other and with the attached hapten. 2,4-Dinitrophenol (DNP) was selected as model hapten, fluorescein as label, and S-sulfonate groups as hydrophilic residues. The properties of the DNP-insulin A-chain-fluorescein **conjugate** (DNP-Ins-Fl) were compared to those of a DNP deriv. labeled with a single fluorescein moiety via a small lysine spacer (DNP-Lys-Fl). The DNP-Ins-Fl **conjugate** exhibited a 3-fold lower nonspecific adsorption to **immobilized** non-immune Ig contributing to an approx. 3-fold more efficient displacement from the binding sites of an **immobilized** monoclonal anti-DNP antibody by the antigen DNP-lysine. Furthermore, at equimolar concns. the DNP-Ins-Fl generated a 2.6-fold higher fluorescent signal than DNP-Lys-Fl. Due to these properties of DNP-Ins-Fl, DNP-lysine could be detected with an approx.

10-fold higher sensitivity compared to DNP-Lys-Fl as labeled antigen. The use of DNP-Ins-Fl as reporter molecue in a competitive fluoroimmunoassay allowed the quant. detn. of picomole amts. of DNP-lysine.

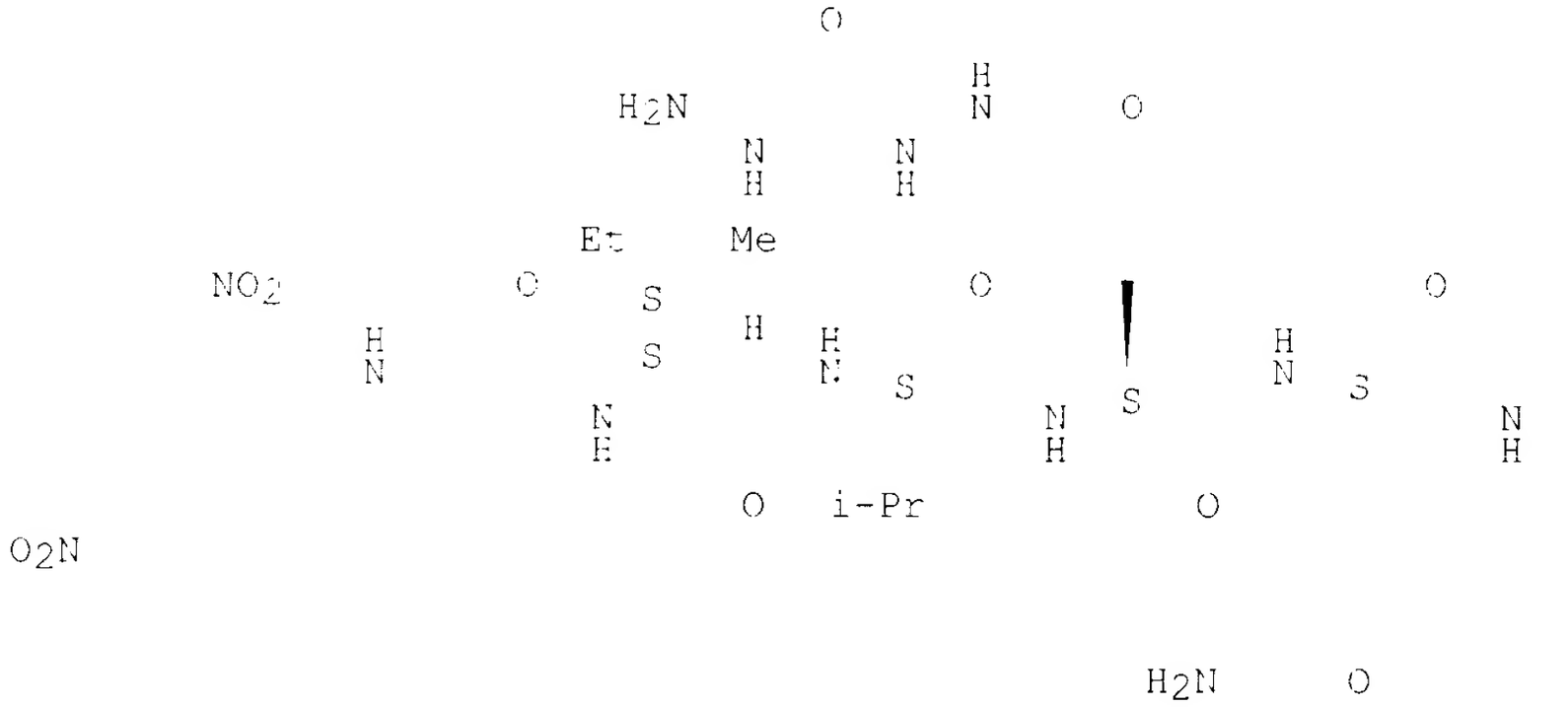
IT **134664-50-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with FITC)

RN 134664-50-9 HCAPLUS

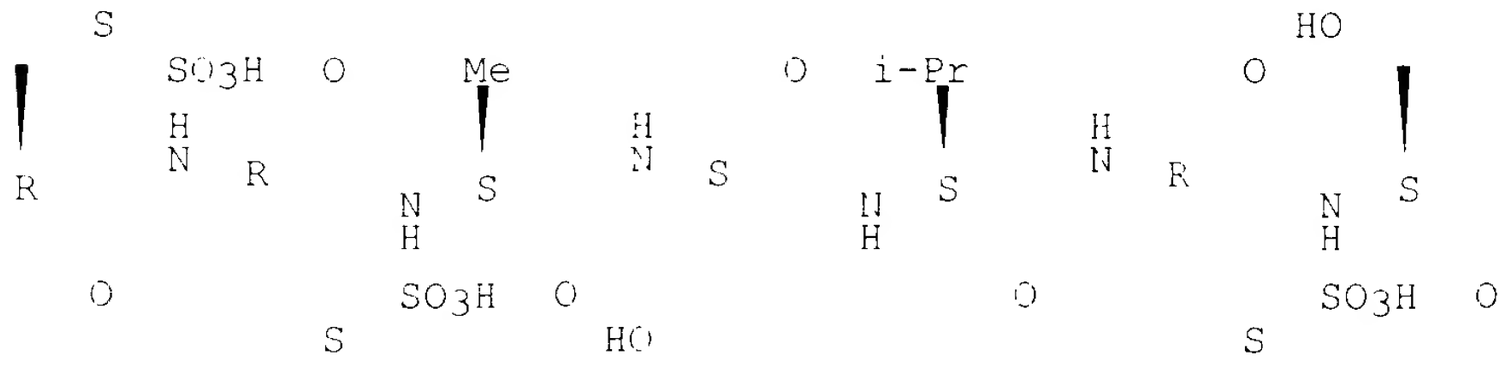
CN Insulin (cattle-A reduced), N-(2,4-dinitrophenyl)-, tris[2-(hydrazinocarbonyl)hydrazide], 6,7,11,20-tetrakis(hydrogen sulfate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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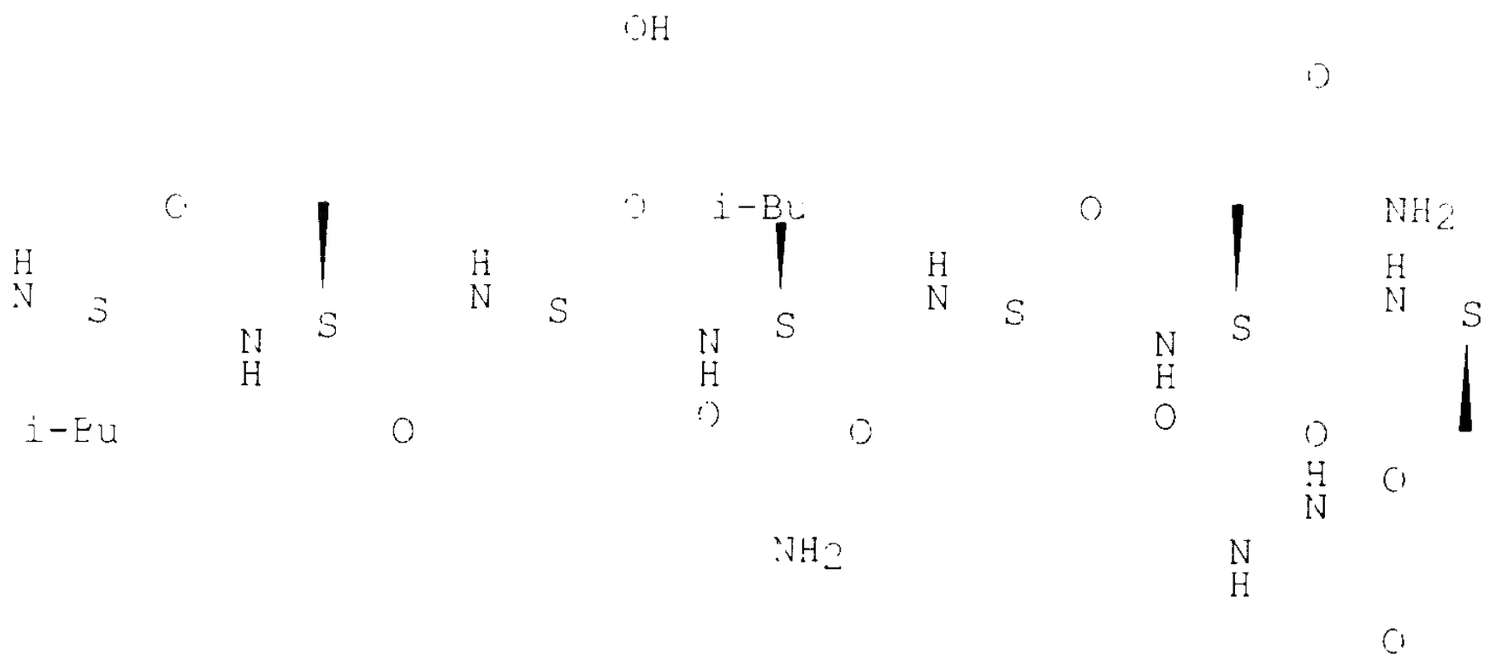

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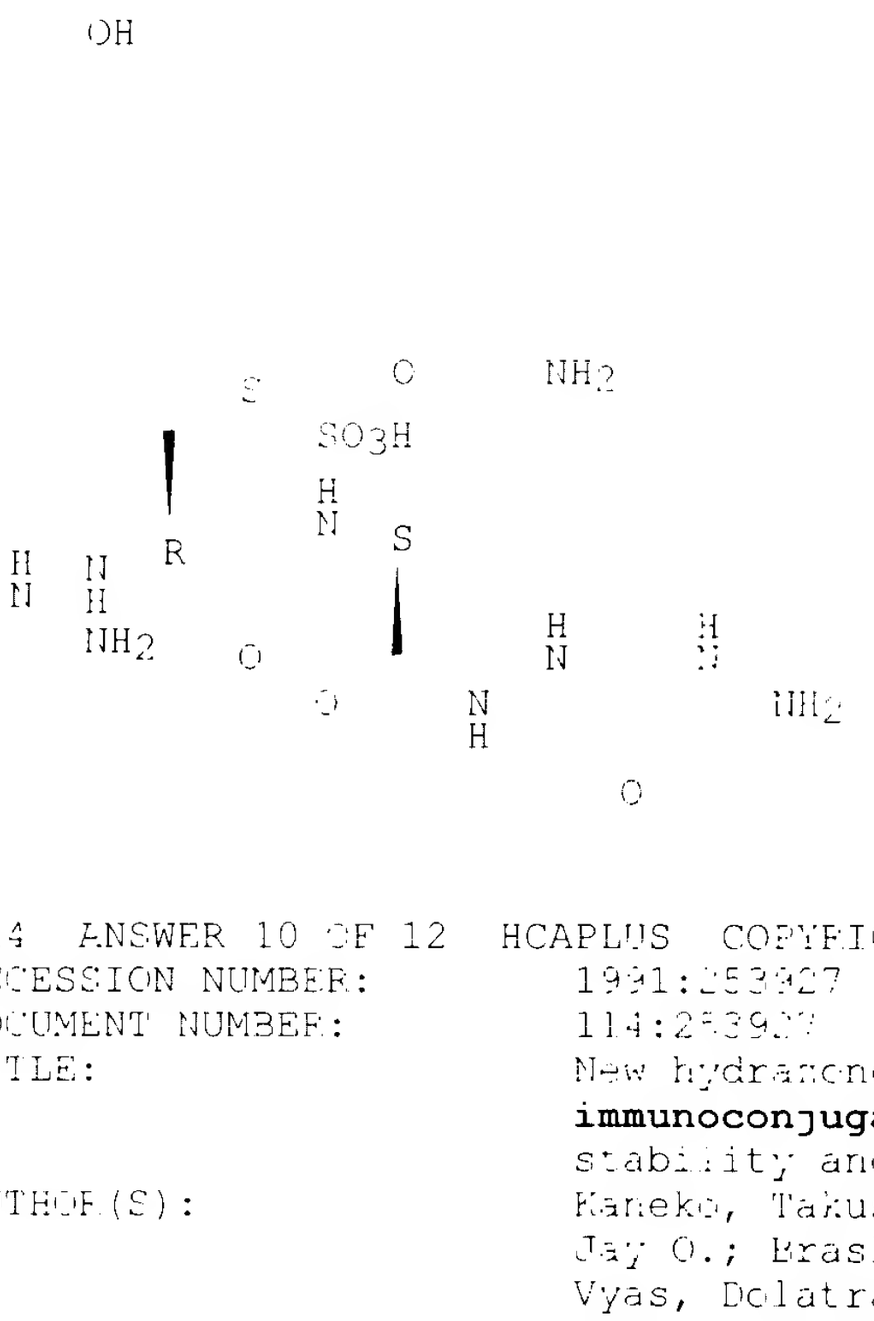


L14 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:253927 HCAPLUS
DOCUMENT NUMBER: 114:253927
TITLE: New hydrazone derivatives of Adriamycin and their **immunoconjugates** - a correlation between acid stability and cytotoxicity
AUTHOR(S): Kaneko, Takushi; Willner, David; Monkovic, Ivo; Knipe, Jay O.; Braslawsky, Gary R.; Greenfield, Robert S.; Vyas, Dolatrai M.
CORPORATE SOURCE: Bristol-Myers Squibb Co., Wallingford, CT, 06492-7660, USA
SOURCE: Bioconjugate Chemistry (1991), 2(3), 133-41
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal

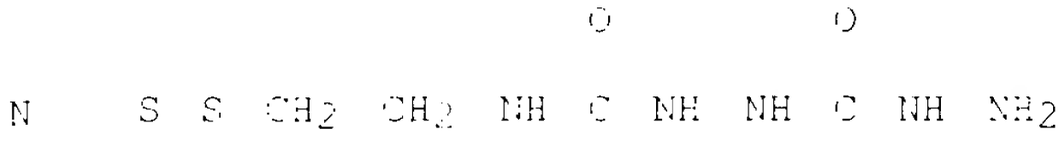
LANGUAGE: English

AB New N-substituted hydrazine linkers were synthesized and their hydrazone derivs. of adriamycin were prepd. The adriamycin derivs. were **conjugated** with a monoclonal antibody, 5E9. The release rate of adriamycin from the hydrazones and from some of the **conjugates** was studied, and their relationship to the cytotoxicity against 5E9-pos. Daudi cells was investigated.

IT **133701-19-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation of, with adriamycin, hydrazone from)

RN 133701-19-6 HCAPLUS

CN Carbonic dihydrazide, 2-[[[2-(2-pyridinyldithio)ethyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:199302 HCAPLUS
DOCUMENT NUMBER: 98:199302
TITLE: Curing of poly(glycidyl ether) resins
INVENTOR(S): Sponseller, David B.; Melby, Earl G.; Fabris, Hubert J.
PATENT ASSIGNEE(S): General Tire and Rubber Co., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4377620 | A | 19830322 | US 1982-382871 | 19820528 |

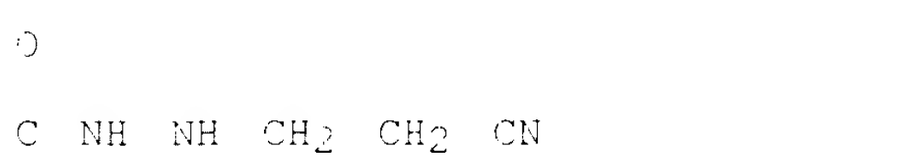
PRIORITY APPLN. INFO.: US 1982-382871 19820528

AB Cyanoalkylated hydrazides are useful as curing agents for epoxy resins, having useful pot life and showing fast cures. Thus, 1.68 g bis(cyanoethyl)carbohydrazide [85785-04-2] was mixed with 3.7 g Epon 828 [25068-38-6] to give a compn. having gel time 2.1 min at 149.degree. and room temp. pot life 6 days.

IT **85785-03-1**
RL: MOA (Modifier or additive use); USES (Uses)
(**crosslinking** agents, for epoxy resins)

RN 85785-03-1 HCAPLUS

CN Carbonic dihydrazide, 2-(2-cyanoethyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:61[illegible]98 HCAPLUS
DOCUMENT NUMBER: 81:[illegible]
TITLE: Aqueous dispersions of copolymers with carbonyl groups and containing hydrazine derivatives
INVENTOR(S): Ley, Gregor; Penzel, Erich; Rebafka, Walter; Bott, Kaspar
PATENT ASSIGNEE(S): BASF A.-G., Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., [illegible] pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

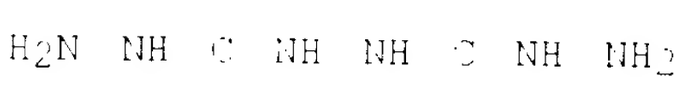
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 3816 | A1 | 19790822 | EP 1979-100168 | 19790119 |
| EP 3816 | B1 | 19810401 | | |
| F: BE, CH, DE, FR, GB, IT, NL, SE | | | | |
| US 4250070 | A | 19810210 | US 1979-3965 | 19790116 |
| CA 1151736 | A1 | 19830809 | CA 1979-320124 | 19790124 |
| DK 7[illegible]617 | A | 19790[illegible]7 | DK 1979-317 | 19790125 |
| FI [illegible]1795 | B | 19[illegible]80111 | | |
| DE 151[illegible]95 | C | 19[illegible]90[illegible]13 | | |
| NO 7900255 | A | 19790727 | NO 1979-255 | 19790125 |
| NO 155695 | B | 19870202 | | |
| NO 155695 | C | 19870513 | | |
| ES 477135 | A1 | 19791201 | ES 1979-477135 | 19790125 |
| AT 79[illegible]0557 | A | 19801015 | AT 1979-557 | 19790125 |
| AT 36[illegible]586 | B | 19810525 | | |
| JP 54110248 | A2 | 19790829 | JP 1979-7291 | 19790126 |
| JP 61006861 | B4 | 19860301 | | |

PRIORITY APPLN. INFO.: DE 1978-2803258 197-01-26

AB Aq. coating dispersions of reaction products of polycarboxylic acid hydrazides, bis(semicarbazides), or CO(NHNH2)2 with aldehyde or ketone carbonyl group-contg. vinyl polymers are stabilized against hydrolysis during storage by addn. of 0.0002-0.02 mol Cu, Fe, Mn, V, Zn, Cr, and(or) Ni per mol hydrazine deriv.; the metal salts are also **crosslinking** catalysts. Thus, 200 parts 17.5% aq. 25:50:25 succinic dihydrazide-glutaric dihydrazide-adipic dihydrazide dispersion and 0.06 part CuSO4 were added to a copolymer dispersion, prepd. from Me acrylate 37%, Bu acrylate 90, acrylic acid 10, and acroleir 25 parts, to give a storage-stable dispersion. A room temp.-dried coating film swelled in DMF picking up 110-210% of its wt. in 1 day, but did not dissolve.

IT **1617-13-6D**, reaction products with carbonyl group-contg. polymers
RL: TEM (Technical or engineered material use); USES (Uses)
(coatings, stabilization of, with transition metal salts)

RN 1617-13-6 HCAPLUS
CN 1,2-Hydrazinedicarboxylic acid, dihydrazide (9CI) (CA INDEX NAME)



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L2              7 S L1 AND ?HYDRAZINE?
                SELECT FN L2 2

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L4              5 S L2 AND L3

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L5                STR
L6              3 S L5
L7            609 S L5 FUL

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RING(S) ARE ISOLATED OR EMBEDDED
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NUMBER OF NODES IS   7

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L13          122 SEA FILE=HCAPLUS ABB=ON  L12
L14           12 SEA FILE=HCAPLUS ABB=ON  L13 AND (?CROSSLINK? OR ?BIFUNCT? OR
                 IMMOBILI? OR ?CONJUGAT?)
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